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Inventor:	Istvan TOTH, et al.	Docket No.:	26979-0005
Serial No.:	10/676,436	Group Art Unit:	1614
Filing Date:	June 30, 2003	Examiner:	Not as yet assigned
For:	**DELIVERY SYSTEMS**		

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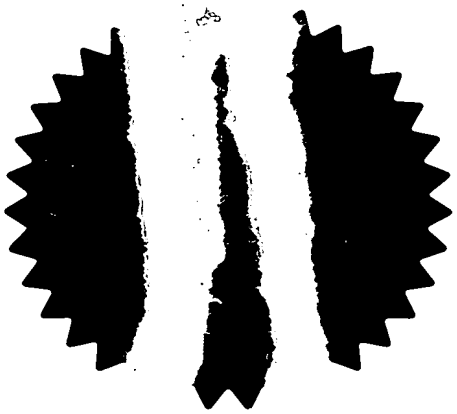

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04 JAN 2001

1.	Your reference	GRIZ / P23976GB
2.	Patent application number *(The Patent Office will fill in this part)*	**0100115.5**
3.	Full name, address and postcode of the or of each applicant *(underline all surnames)*	Alchemia Pty Ltd 3 Hi-Tech Court Brisbane Technology Park Eight Mile Plains QLD 4113 Australia 04JAN01 E595291-2 D02866 P01/7700 0.00-0100115.5
	Patents ADP number *(if you know it)*	08053746001
	If the applicant is a corporate body, give the country/state of its incorporation	Australia
4.	Title of the invention	DELIVERY SYSTEMS
5.	Name of your agent *(if you have one)* "Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*	**ERIC POTTER CLARKSON** **PARK VIEW HOUSE** **58 THE ROPEWALK** **NOTTINGHAM** **NG1 5DD**
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6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and *(if you know it)* the or each application number	Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*

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a) *any applicant named in part 3 is not an inventor; or*
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Statement of inventorship and right to grant of a patent *(Patents Form 7/77)*	NO
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Request for substantive examination *(Patents Form 10/77)*	NO
Any other documents *(please specify)*	

11. I/We request the grant of a patent on the basis of this application.

Eric Potter Clarkson

Signature

ERIC POTTER CLARKSON

Date

3 January 2001

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DELIVERY SYSTEMS

This invention relates to delivery systems for pharmaceutically-active agents. In particular, the invention relates to compounds comprising a carbohydrate moiety and/or a lipid moiety, which are useful as delivery agents.

BACKGROUND OF THE INVENTION

It will be clearly understood that, although a number of prior art publications are referred to herein, this reference does not constitute an admission that any of these documents forms part of the common general knowledge in the art, in Australia or in any other country.

The successful development of any medicinal compound relies on specific and potent pharmacological activity combined with efficient delivery of the molecule to its target site. Many potential drugs and medicinal peptides fail to reach the marketplace due to poor bioavailabillity.

Poor oral absorption presents a significant barrier to the clinical success of many drugs, particularly peptides. Drug delivery strategies seek to overcome the physical and chemical properties responsible for this poor bioavailabillity, including molecular size, charge, hydrophilicity, hydrogen bonding potential and enzymatic lability. There are only a few reliable examples of therapeutic levels for peptides and proteins being achieved via the oral route.

A number of approaches have been employed to improve oral bioavailabillity for therapeutic molecules. These include the use of penetration enhancers, which alter membrane permeability non-specifically [Lee, V.H.L.; Yamamoto, A.; Kompella, U.B. *Crit. Rev. Ther. Drug Carrier Syst.*, **1991**, *8*, 91-192.], the use of drug delivery systems such as liposomes, microparticles and microemulsion systems which protect the drug from the environment, and the use of

prodrugs which modify the drug molecule itself to impart the desired physicochemical properties.

It is believed that the more lipophilic the molecule, the faster and more completely a drug molecule crosses the intestinal barrier. There is a danger, however, of making a drug too lipophilic for epithelial transport. Results suggest that there is a degree of lipophilicity which is "optimal" for absorption. Highly lipophilic drugs suffer from poor aqueous solubility, which is also necessary for successful oral uptake.

Occasionally hydrophilic drug molecules show unexpectedly high rates of oral absorbtion. Two mechanisms have been proposed to explain this effect. Active transport systems can be accessed by some molecules resulting in the "pumping" of hydrophilic molecules into the body. Alternatively, ion pair transport has been proposed to explain the unexpected absorption of highly hydrophilic drugs such as the tetracyclines, which are charged over the range of physiological conditions, and are generally lipid insoluble [Meyer, J.D.; Manning, M.C.; Hydrophobic Ion Pairing: Altering the Solubility Properties of Biomolecules. *Pharm. Res.*, **1998**, *15*, 188-193]. The interaction of such drugs with endogenous counter-ions in effect "buries" the charge within the ion pair, forming a neutral species, which may be able to traverse the epithelium. Hydrophobic ion pairing represents an inexpensive and reversible means by which to modify the physicochemical properties of a drug without the need for irreversible chemical modification [Neubert, R. Ion Pair Transport Across Membranes. *Pharm. Res.*, **1989**, *6*, 743-747].

The ability to form an ion pair and the success of improving transport by this approach depends very greatly on the physicochemical properties of both the drug and the counter-ion.

An ion pair can be defined as a neutral species formed by electrostatic attraction between oppositely

charged ions in solution, which are often sufficiently lipophilic to dissolve in non-aqueous solvents [Quintanar-Guerrero, D.; Allemann, E.; Fessi, H.; Doelker, E. Applications of the Ion-Pair Concept to Hydrophilic Substances with Special Emphasis on Peptides. *Pharm. Res.*, **1997**, *14*, 119-127].

The lipophilicity of hydrophilic ionised drugs can be increased by ion pair formation with lipophilic counter-ions such as hexylsalicylate or decylsulphate. It appears that ion pair formation only affects the partition and transport of hydrophilic drugs which are charged in the media in which ion pairing takes place.

Although counter-ions such as alkylsulphates, trichloroacetate and alkylcarbonates have been used for ion pairing, it has been suggested that these counter-ions are too irritant to the gut at the required dosages [Neubert, et al op. cit.]. *Pharm. Res.*, **1989**, *6*, 743-747 and references here-in]. Counter-ions need to have the following properties: high lipophilicity, sufficient solubility, physiological compatibility and metabolic stability. Suitable counter-ions include alkanoic acids [Green, P.G.; Hadgraft, J. *Int. J. Pharm.*, **1987**, *37*, 251-255] and alkylated salicylic acids [Neubert, R. Ion Pair Transport Across Membranes. *Pharm. Res.*, **1989**, *6*, 743-747].

It was initially supposed that the two components of an ion pair traverse lipid membranes at an equimolar ratio. However, the mechanism may be more complex. Experiments based on lipophilic counter-ions for cationic drug transport showed that the counter-ions accumulated in the membrane, and that, as a result, more hydrophilic drug molecules than counter-ions were transported. Transport of the complete ion pair was also demonstrated. (Neubert et al. 1989 op.cit.]. A similar mechanism has been proposed for the transport of anionic drugs [Hadgraft, J.; Wotton, P.K.; Walters, K.A. *J. Pharm. Pharmacol.*, **1985**, *37*, 757-727].

The approaches discussed thus far are based on increasing lipophilicity for enhanced transport by passive diffusion via the transcellular pathway. An alternative strategy is to exploit the numerous active transport mechanisms present in the gastrointestinal mucosa. Strategies have been designed to improve the bioavailability of poorly absorbed drugs and peptides so that they can be absorbed by specialised intestinal transporters.

Conjugation of a saccharide moiety to a poorly absorbed drug improves its solubility in aqueous media due to the poly-hydroxyl nature of sugars. In addition, sugar conjugation may allow passage of the sugar-drug conjugate across the gut via the SGLT-1 glucose transporter [Gould, G.W.; Holman G.D. The Glucose transporter family: structure, function and tissue-specific expression. *Biochem. J.*, **1993**, *295*, 329-341]. The effectiveness of this approach has been demonstrated by conjugation of a glucose derivative to a tetrapeptide not normally transported by PepT1 [Nomoto, M.; Yamada, K.; Haga, M.; Hayashi, M. Improvement of Intestinal Absorption of Peptide Drugs by Glycosylation: Transport by the Sodium Ion-Dependent D-Glucose Transporter. *J. Pharm. Sci.*, **1998**, *87*, 326-332]. Interestingly, the configuration at the anomeric centre of the sugar was found to affect the rate of transport: A β-anomeric linkage was preferred over the α-configuration. Subsequently, further evidence was presented for glycosides of paracetamol [Mizuma, T.; Nagamine, Y.; Dobashi, A.; Awazu, S. Factors that cause the β-anomeric preference of Na+/glucose cotransporter for intestinal transport of monosaccharides conjugates. *Biochim. Biophys. Acta*, **1998**, *1381*, 340-346]. Glucose conjugates were transported more efficiently than galactose conjugates, with the β-*trans*-anomeric configuration preferred in both cases. Galactose conjugates with the α-*cis*-configuration were not transported at all.

We have previously demonstrated the utility of conjugating lipoamino acids or lipoaminosaccharide constructs to drug molecules through a covalent bond (Australian Provisional Patent Application No. PR0844 filed 18 October 2000; (Toth et al., 1993; Toth and Gibbons, British Patent Application No. 9215780.9 (24 July, 1992); Toth and Gibbons, European Patent Application No. 93917902.4). These compounds provide an excellent delivery system, but require the chemical conjugation of the drug molecule to the delivery system.

We now propose the use of lipoamino acids and lipoaminosaccharide conjugates as an ionic delivery system in which the drug molecule and the delivery system form an ionic complex. This system does not require the chemical conjugation of the drug molecule, and therefore will not alter the pharmacological properties of the drug molecule. In addition, this method of delivery can be used to target either passive or active transport mechanisms. The proposed delivery system is readily optimised for hydrophilic drug molecules, peptides and proteins, and offers significant benefits in terms of regulatory approval. We believe that this is the first example of the use of non-covalently linked lipoamino acids and lipoamino saccharides for drug delivery.

SUMMARY OF THE INVENTION

In a first aspect, the invention provides a pharmaceutical agent of general formula I:

$$r[D^{(nz)}]\ p[(W_q\text{-}S\text{-}X\text{-}L)^{(my)}]$$

formula I

in which D is a therapeutically useful molecule, such as a drug, peptide, protein, or nucleic acid;

r, p, n and m are independently integers greater than or equal to 1;

n and m represent the overall magnitude of the charge on the molecules; and

z and y are charges, either positive (+) or negative (-), such that when z is positive, y must be negative and *vice versa*;

and $[(Wq\text{-}S\text{-}X\text{-}L)^{(my)}]$ is a carrier construct, in which

X is a linker, which may optionally be absent, or is selected from 2 to 10 atom spacers, which may be substituted or unsubstituted, branched or linear;

S is a mono- or oligosaccharide, which may be of natural or synthetic origin;

L is a lipidic moiety, as defined herein;

W may be absent, or is a 3 to 10 atom alkyl or heteroalkyl spacer, which may be branched or linear, and is substituted with one or more functional groups, each of which is charged or is capable of carrying a charge under physiological conditions; and

q is an integer, which is 0 when W is absent, or ranges from 3 to the number of hydroxyls available for substitution on the sugar moiety; for example when S is a monosaccharide, q may be 0, 3 or 4; when S is a disaccharide q may be 0 or 3 to 7.

In the case of biological molecules, for example DNA, n and m may be relatively high or indeterminate. It will be apparent that the values n and m are not required to be equal, and that there is no requirement for the complex to be neutral. It will be further apparent that there is no requirement for the drug and carrier to be in stoichiometric amounts, and that the drug may be present in large excess over the carrier or *vice versa*, if this is required to effect efficient delivery of the drug molecule.

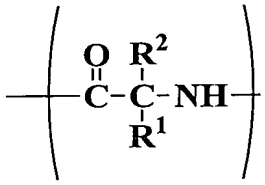
The linker X may be attached to the sugar S through the glycosidic position, or via any other suitable position on the sugar, by methods known in the art. Examples of such linkages include, but are not limited to O-glycoside, C-glycoside, N-glycoside, S-glycoside, amide, urea, thiourea, carbamate, thiocarbamate, carbonate, ether and ester bonds.

Similarly the linker X may be attached to the lipidic moiety L by methods known to those skilled in the art, including but not limited to amide, ester, ether, imine, carbamate, urea, thiourea, or carbonate linkages.

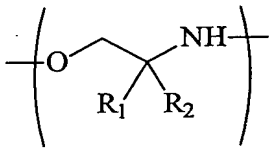
Examples of suitable functional groups W include, but are not limited to, amidine, guanidinium, carboxylate, tetrazole, hydroxamic acid, hydrazide, amine, sulfate, phosphonate, phosphate, and sulfonate. It will be apparent that these functional groups may be the same or different, and may be of differing charge, so as to confer suitable properties on the carrier molecule.

The lipidic moiety L is composed of:

(a) any combination of 1 to 4 lipoamino acids and/or lipoamino alcohols, of general formula IIa or IIb



IIa



IIb

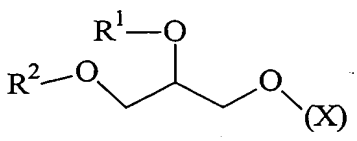
in which each of R^1 and R^2 may independently be:

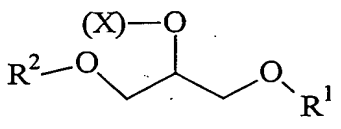
(i) hydrogen, or

(ii) a linear or branched chain alkyl or alkenyl group having 4 to 24 carbon atoms, which may optionally be substituted, provided that the substituents do not significantly adversely affect the lipophilic nature of the group,

with the proviso that both R^1 and R^2 cannot be hydrogen at the same time;

(b) a glycerol-based lipid of general formula IIIa or IIIb



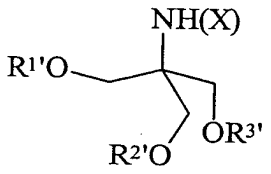


IIIa **IIIb**

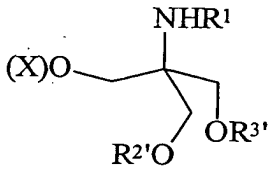
in which R^1 and R^2 are as defined in general formula IIa, and

X is a linker group, as defined in general formula I; or

(c) a trishydroxymethylmethylamine-based lipid of general formula IVa or IVb



IVa



IVb

in which $R^{1'}$, $R^{2'}$ and $R^{3'}$ are independently hydrogen or a linear or branched chain alkyl or alkenyl group having 4 to 24 carbon atoms, which may optionally be substituted, provided that the substituents do not significantly adversely affect the lipophilic nature of the group and X is as defined in general formula I;

with the proviso that only one of R^1, R^2 and R^3 can be hydrogen.

The lipidic moiety L may optionally contain one or more charged functional groups, such as amidine, guanidinium, carboxylate, tetrazole, hydroxamic acid, hydrazide, amine, sulfate, phosphonate, phosphate, or sulfonate. It will be apparent that these functional groups may be the same or different, and may be of differing charge, so as to confer suitable properties on the carrier molecule.

In a preferred embodiment, the first aspect of the invention provides an agent of general formula I in which the sugar S is a mono-, di- or tri-saccharide, and the lipidic moiety is one to three lipoaminoacids of general formula IIa or IIb.

In a particularly preferred embodiment the agent is piperacillin / 2-acetamido-2-deoxy-*N*-(1-amino-(R/S)-dodecoyl)-β-D-gluco-pyranosylamine ionic complex.

In a second aspect, the invention provides a carrier construct of general formula V:

$$[(W)_q\text{-}S\text{-}X\text{-}L)^{(my)}]$$

formula V

in which W, S, X, L, m, q and y are as defined in General Formula I.

In a third aspect, the invention provides a method of preparing a carrier construct of general formula V, comprising the step of forming a covalent bond between the sugar S and the linker X or the lipid L, in which the bond between S and X is an O-glycoside, C-glycoside, N-glycoside, S-glycosides, amide, urea, thiourea, carbamate, thiocarbamate, carbonate, ether or ester bond, and the bond between X and L is an amide, ester, ether, imine, carbamate, urea, thiourea, or carbonate bond.

In a fourth aspect, the invention provides a composition comprising a pharmaceutical agent according to the invention together with a pharmaceutically-acceptable carrier.

In a fifth aspect, the invention provides a method of preparation of a pharmaceutical agent of general formula I, comprising the step of mixing a drug molecule D with a carrier construct of general formula V in solution, followed by removal of the solvent(s) to provide a homogeneous mixed salt.

In a sixth aspect, the invention provides a method of delivery of a therapeutically useful molecule by oral administration, comprising the step of administering the molecule to a subject in need of such treatment in the form of a pharmaceutical agent of general formula I.

The mammal may be a human, or may be a domestic

or companion animal. While it is particularly contemplated that the compounds of the invention are suitable for use in medical treatment of humans, they are also applicable to veterinary treatment, including treatment of companion animals such as dogs and cats, and domestic animals such as horses, cattle and sheep, or zoo animals such as felids, canids, bovids, and ungulates.

Methods and pharmaceutical carriers for preparation of pharmaceutical compositions are well known in the art, as set out in textbooks such as Remington's Pharmaceutical Sciences, 19th Edition, Mack Publishing Company, Easton, Pennsylvania, USA.

The carrier or diluent, and other excipients, will depend on the route of administration, and again the person skilled in the art will readily be able to determine the most suitable formulation for each particular case.

For the purposes of this specification it will be clearly understood that the word "comprising" means "including but not limited to", and that the word "comprises" has a corresponding meaning.

DETAILED DESCRIPTION OF THE INVENTION:

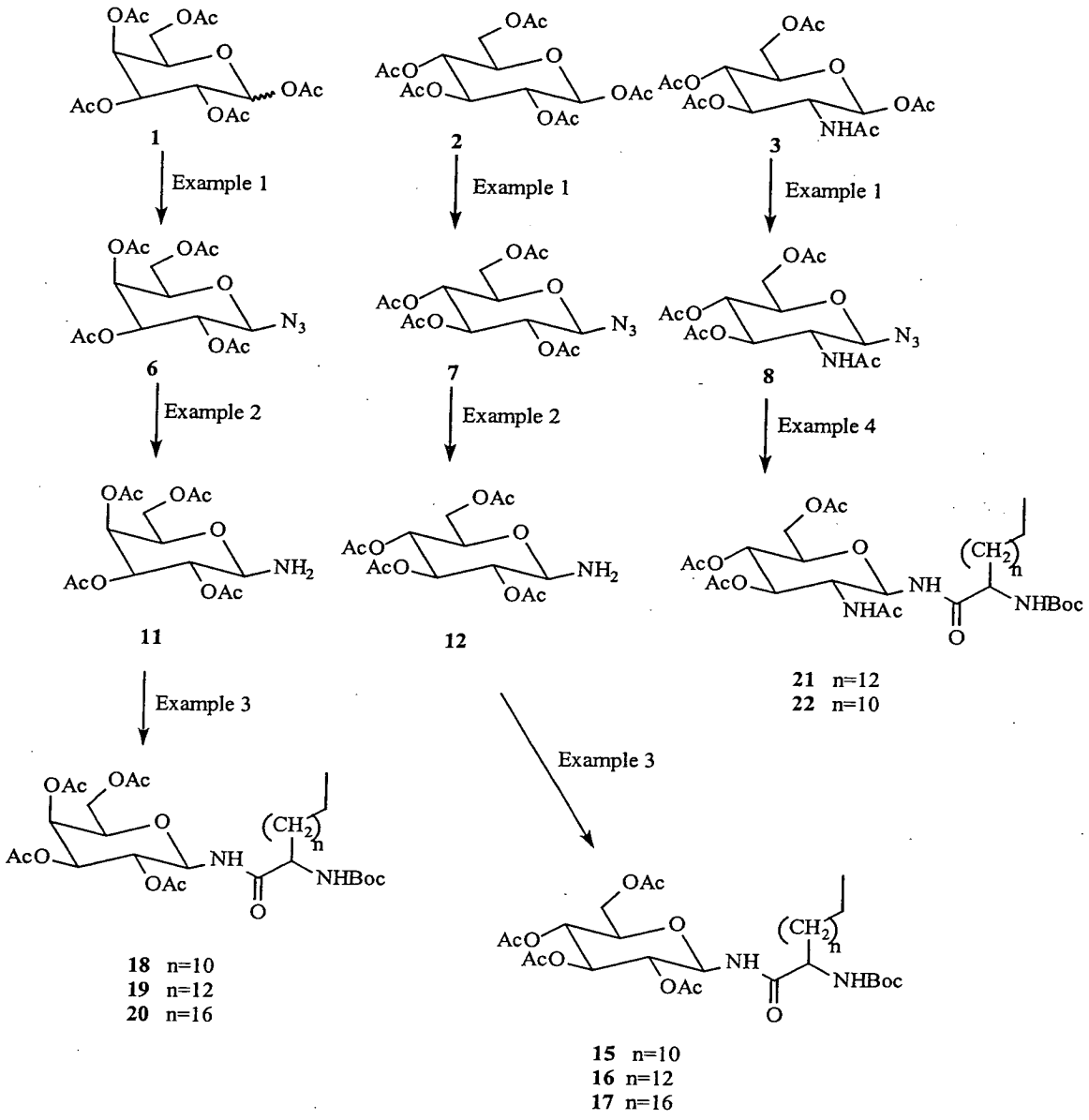
The invention will now be described in detail by way of reference only to the following non-limiting examples.

Examples 1 to 7 inclusive provide methods for the preparation of amide-linked mono, di and tri-saccharide-lipoamino acid complexes. The general reaction schemes are set out in Schemes 1 and 2, which relate to Example 1 to 4, Scheme 3, which follows on from Scheme 2 and relates to Examples 5 and 6, and Scheme 4, which follows on from Scheme 1, and relates to Examples 5 to 7.

Examples 8 to 16 inclusive provide methods for the preparation of complexes in which lipids are alternatively linked to the anomeric position of

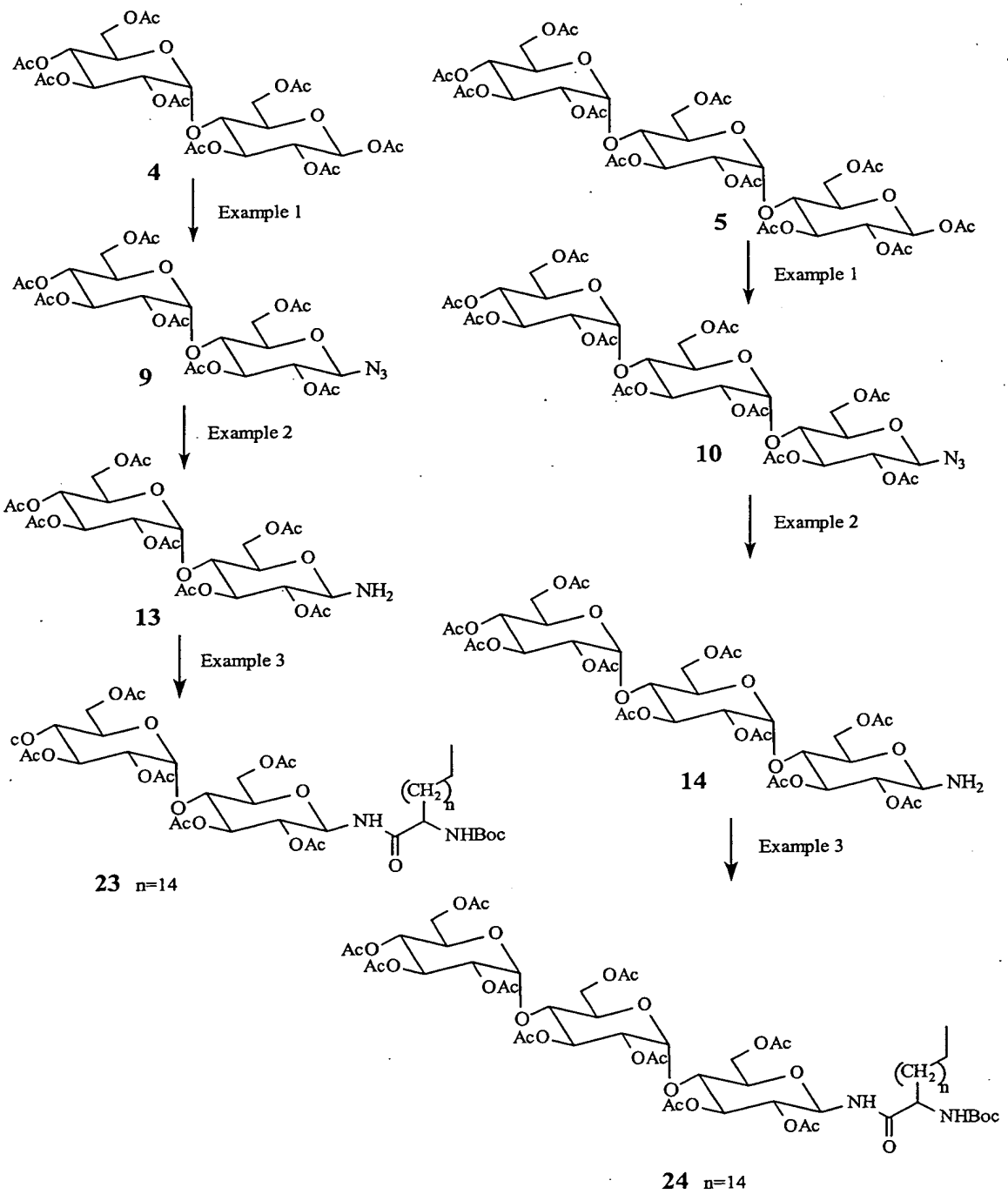
monosaccharides.

General schemes for synthesis of protected amide-linked charged monosaccharide- and polysaccharide lipoamino acid conjugates respectively are set out below.



Scheme 1

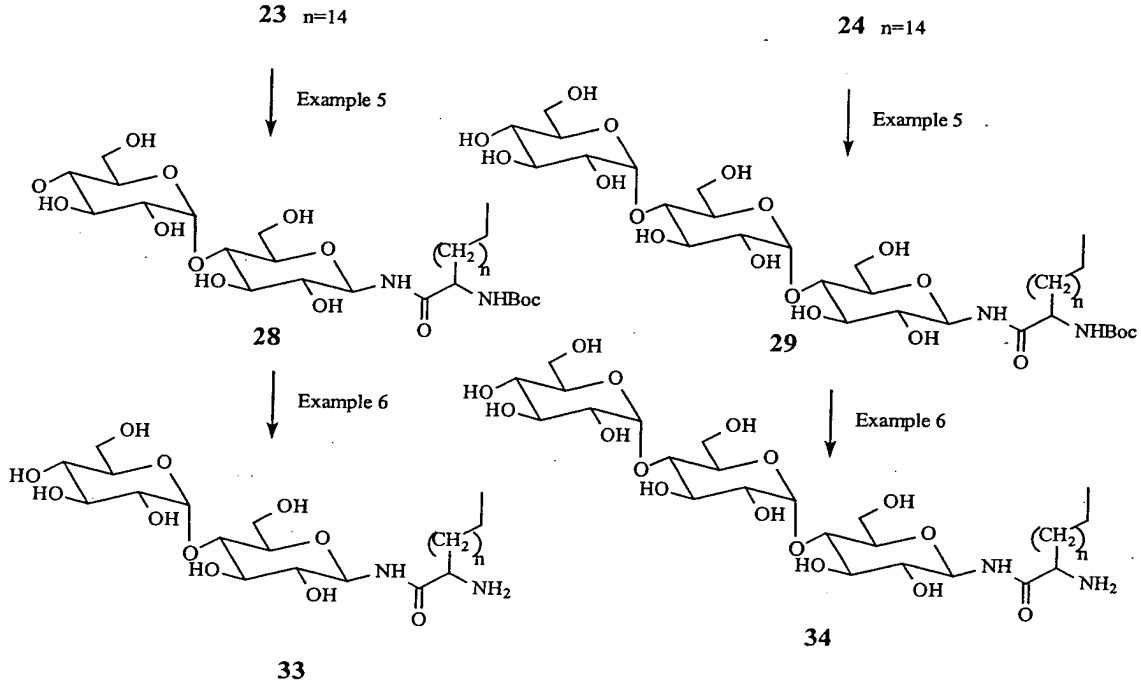
Monosaccharide-lipoamino acid conjugates



Scheme 2

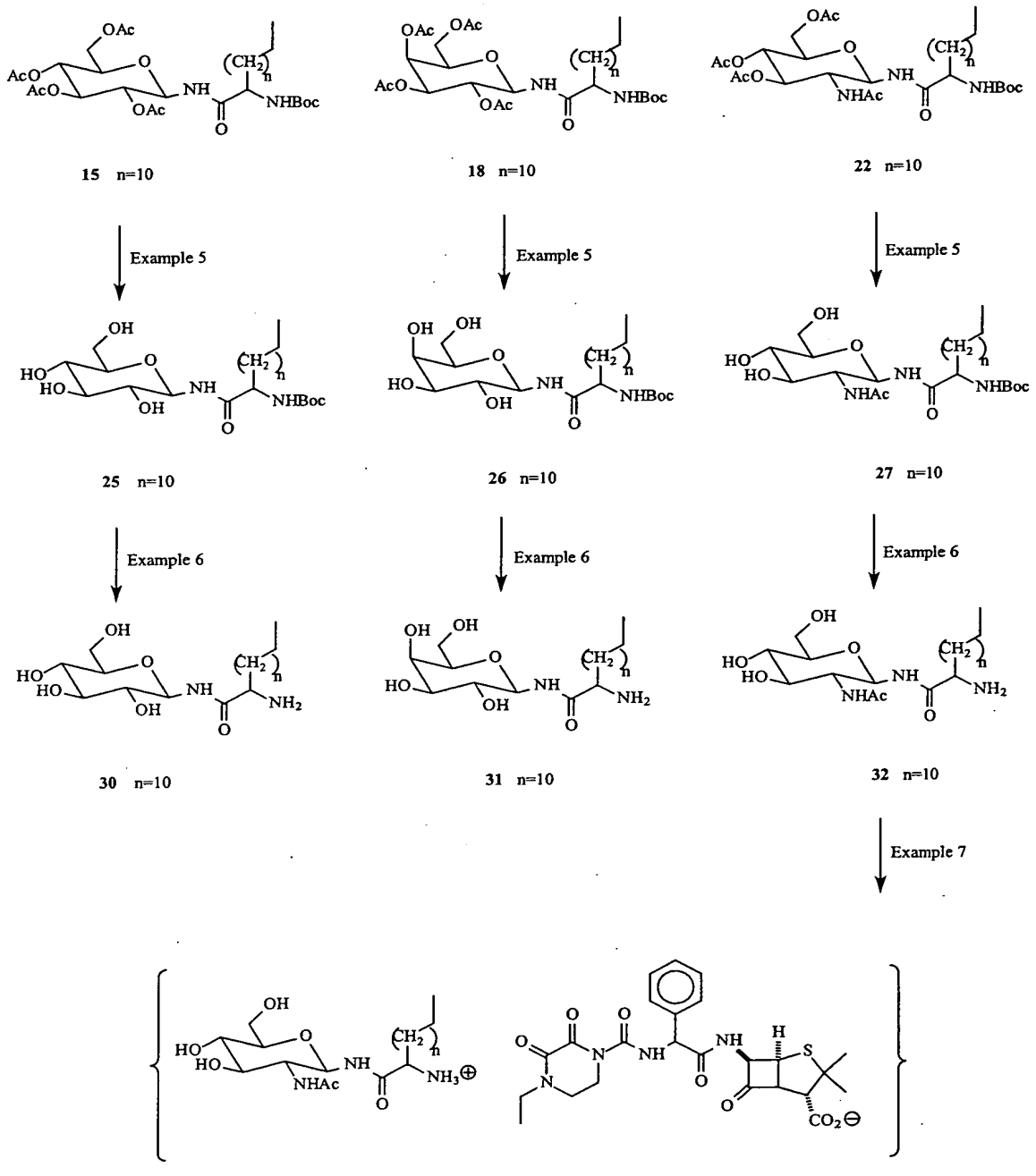
Polysaccharide-lipoamino acid conjugates

General scheme for deprotection of amide-linked charged oligosaccharide lipoamino acids.



Scheme 3

General scheme for deprotection of amide-linked charged monosaccharide lipoamino acid complexes and preparation of charged glycolipid - drug complexes.



Scheme 4

Example 1

2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl azide (**6**)

1,2,3,4,6-penta-*O*-acetyl-α/β-D-galactopyranose (**1**) (10.0 g, 25.6 mmol) was dissolved in abs. CH_2Cl_2 (100 ml). Trimethylsilyl azide (7.38 g, 64.1 mmol) and tin(IV) chloride (3.34 g, 12.8 mmol) were added to the solution, which was then stirred overnight. The reaction mixture was then diluted with CH_2Cl_2 (250 ml), washed with 1M $KF_{(aq)}$ (1 x 250 ml), brine (1 x 250 ml) and $NaHCO_{3(sat,\ aq)}$ (1 x 250 ml). The organic phase was dried over $MgSO_4$, filtered and evaporated. Recrystallisation from ethyl acetate:hexane 1:1 (v/v) gave (**6**) (8.62 g, 90%).

R_F = 0.60 hexane:ethyl acetate 1:1 (v/v); ^1H NMR δ 5.41 (d, 1H, H-4), 5.17 (m, 1H, H-2), 5.04 (m, 1H, H-3), 4.60 (d, 1H, H-1, $J_{1,2}$=8.7 Hz), 4.19 (m, 2H, H-6, H-6'), 4.00 (m, 1H, H-5), 2.15, 2.08, 2.05, 1.98 (4s, 12H, 4Ac); FAB MS $C_{14}H_{19}N_3O_9$ (373.32) m/z (%) 396 $[M+Na]^+$ (100).

Cognate preparation of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl azide (**7**)

re-crystallisation from ethyl acetate:hexane 2:1 (v/v) gave (**7**) (7.87 g, 82%).

R_F = 0.55 hexane:ethyl acetate 1:1 (v/v); ^1H NMR δ 5.21, 5.09 (2t, 2H, H-3, H-4), 4.94 (t, 1H, H-2), 4.65 (d, 1H, H-1, $J_{1,2}$=8.8Hz), 4.27, 4.15 (2m, 2H, H-6, H-6'), 3.81 (m, 1H, H-5), 2.09, 2.07, 2.02, 1.99 (4s, 12H, 4Ac); FAB MS $C_{14}H_{19}N_3O_9$ (373.32) m/z (%) 396 $[M+Na]^+$ (20), 331 $[M-N_3]^+$ (100).

Cognate preparation of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl azide (**8**)

R_F = 0.50 ethyl acetate; yield 87%; ^1H NMR δ 5.70 (d, 1H, NH), 5.24 (t, 1H, H-3), 5.09 (t, 1H, H-4), 4.76 (d, 1H, H-1, $J_{1,2}$=9.1 Hz), 4.25, 4.16 (2m, 2H, H-6, H-6'), 3.90 (m, 1H, H-2), 3.79 (m, 1H, H-5), 2.09, 2.03, 2.02, 1.97 (4s,

12H, 4Ac); FAB MS $C_{14}H_{20}N_4O_8$ (372.33) m/z (%) 373 $[M+H]^+$ (100), 395 $[M+Na]^+$ (30), 330 $[M-N_3]^+$ (97).

Cognate preparation of *O*-[2',3',4',6'-tetra-*O*-acetyl-α-D-glucopyranosyl(1'→4)]-2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl azide (**9**)

R_F = 0.30 hexane:ethyl acetate 8:7 (v/v); yield 84%; ^1H NMR δ 5.41 (d, 1H, H-1', $J_{1',2'}$=4.0 Hz), 4.85 (dd, 1H, H-4'), 4.78 (t, 1H, H-2), 4.70 (d, 1H, H-1, $J_{1,2}$=8.7 Hz), 2.15 - 1.99 (7s, 21H, 7Ac); FAB MS $C_{26}H_{35}N_3O_{17}$ (661.57) m/z (%) 684 $[M+Na]^+$ (100), 360 (25).

Cognate preparation of *O*-{*O*-[2'',3'',4'',6''-tetra-*O*-acetyl-α-D-glucopyranosyl(1''→4')]-2',3',6'-tetra-*O*-acetyl-α-D-glucopyranosyl(1'→4)}-1,2,3,6-tetra-*O*-acetyl-β-D-glucopyranosyl azide (**10**)

R_F = 0.70 hexane:ethyl acetate 4:10 (v/v); yield 79%; FAB MS $C_{38}H_{51}N_3O_{25}$ (949.82) m/z (%) 973 $[M+Na]^+$ (100), 945 (38).

Example 2

2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosylamine (**11**)

Palladium catalyst (10% on carbon, 20.0 mg) was added in one portion to a solution of 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl azide (**6**) (500 mg, 1.34 mmol) in abs. methanol (5 ml) under a hydrogen atmosphere. A small amount of abs. THF was added to dissolve the sugar. The solution was allowed to stir for 12 hours. The catalyst was subsequently filtered off, and the solvent evaporated. Purification by column chromatography gave (**11**) (400 mg, 86%).

R_F = 0.30 hexane:ethyl acetate 8:7 (v/v); ^1H NMR δ 5.40 (d, 1H, H-4), 5.04 (m, 2H, H-2, H-3), 4.16 (d, 1H, H-1, $J_{1,2}$=8.0 Hz), 4.10 (m, 2H, H-6, H-6'), 3.99 (m, 1H, H-5), 2.14, 2.07, 2.06, 1.97 (4s, 12H, 4Ac); FAB MS $C_{14}H_{21}NO_9$ (347.32) m/z (%) 370 $[M+Na]^+$ (100).

Cognate preparation of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamine (**12**) from (**7**)

R_F = 0.35 hexane:ethyl acetate 1:1 (v/v); yield 83%; ^1H NMR δ 5.26 (d, 1H, H-3), 5.16 - 5.03 (m, 2H, H-2, H-3), 4.12 (d, 1H, H-1, $J_{1,2}$=8.5 Hz), 4.12 (m, 2H, H-6, H-6'), 3.86 (m, 1H, H-5), 2.11, 2.06, 2.04, 2.01 (4s, 12H, 4Ac); FAB MS $C_{14}H_{21}NO_9$ (347.32) m/z (%) 370 $[M+Na]^+$ (80).

Cognate preparation of *O*-[2',3',4',6'-tetra-*O*-acetyl-α-D-glucopyranosyl(1→4)]-2,3,6-tri-*O*-acetyl-β-D-glucopyranosylamine (**13**) from (**9**)

R_F = 0.50 chloroform:ethyl acetate 1:2 (v/v); yield 72%; ^1H NMR δ 5.43 (d, 1H, H-1'), 4.13 (d, 1H, H-1), 2.14 - 2.00 (7s, 21H, 7Ac); MALDI TOF MS $C_{26}H_{37}NO_{17}$ (635.57) m/z (%) 659 $[M+Na]^+$ (100), 1278 (43).

Cognate preparation of *O*-{*O*-[2'',3'',4'',6''-tetra-*O*-acetyl-α-D-glucopyranosyl(1'→4')]-2',3',6'-tetra-*O*-acetyl-α-D-glucopyranosyl(1'→4)}-1,2,3,6-tetra-*O*-acetyl-β-D-glucopyranosyl-amine (**14**)from (**10**)

R_F = 0.30 hexane:ethyl acetate 6:10 (v/v); yield 66%; FAB MS $C_{38}H_{53}NO_{25}$ (923.82) m/z (%) 925 $[M+H]^+$ (100), 229 (48).

Example 3

2,3,4,6-tetra-*O*-acetyl-*N*-{1-(R/S)-[(*tert*-butoxycarbonyl)amino]dodecyl}-β-D-glucopyranosylamide (**15**).

2-(R/S)-[(*tert*-Butoxycarbonyl)amino]dodecanoic acid (575 mg, 1.44 mmol) and EEDQ (428 mg, 1.72 mmol) were added to a stirred solution of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamine (**12**) (500 mg, 1.44 mmol) in abs. THF (10 ml). The reaction was stirred at 40°C for 6 hours. After evaporation, the residue was purified by column chromatography to give (**15**).

R_F = 0.87 chloroform:methanol 10:2.5 (v/v); yield 68%; ^1H NMR δ 5.31 - 5.22 (m, 2H, H-1, H-3), 5.06 (m, 1H, H-4), 4.93 (m, 1H, H-2), 4.79 (br s, 1H, NH), 4.28 (m, 1H, H-6),

4.13 - 4.05 (m, 2H, H-6', αCH), 3.80 (m, 1H, H-5), 2.06, 2.03, 2.01, 2.00 (4s, 12H, 4Ac), 1.44 (s, 9H, 3 x Boc CH_3), 1.28 - 1.23 (m, 18H, $9CH_2$), 0.87 (t, 3H, CH_3); FAB MS $C_{31}H_{52}N_2O_{12}$ (644.75) m/z (%) 667 $[M+Na]^+$ (10), 777 $[M+Cs]^+$ (100), 545 $[M-Boc+H]^+$ (15).

Cognate preparation of 2,3,4,6-tetra-*O*-acetyl-*N*-{1-(R/S)-[(*tert*-butoxycarbonyl)amino]tetradecyl}-β-D-glucopyranosylamide (**16**) from (**12**) and 2-(R/S)-[(*tert*-Butoxycarbonyl)amino]tetradecanoic acid

R_F = 0.42 hexane:ethyl acetate 1:1 (v/v); yield 64%; ^1H NMR δ 5.28 (m, 2H, H-1, H-3), 5.06 (m, 1H, H-4), 4.97 (m, 2H, H-2, NH), 4.26, 4.11 (2m, 2H, H-6, H-6'), 3.83 (m, 1H, H-5), 2.08, 2.04, 2.02, 1.99 (4s, 12H, 4Ac), 1.42 (s, 9H, 3 x Boc CH_3), 1.25 (m, 22H, $11CH_2$), 0.86 (t, 3H, CH_3); FAB MS $C_{33}H_{56}N_2O_{12}$ (672.80) m/z (%) 695 $[M+Na]^+$ (40), 805 $[M+Cs]^+$ (65), 573 $[M-Boc+H]^+$ (95).

Cognate preparation of 2,3,4,6-tetra-*O*-acetyl-*N*-{1-(R/S)-[(*tert*-butoxycarbonyl)amino]octadecyl}-β-D-glucopyranosylamide (**17**)from (**12**) and 2-(R/S)-[(*tert*-Butoxycarbonyl)amino]hexadecanoic acid

R_F = 0.34 hexane:ethyl acetate 2:1 (v/v); yield 70%; ^1H NMR δ 6.75 (d, 1H, NH), 5.25 (m, 2H, H-1, H-3), 5.07 (dd, 1H, H-4), 4.94 (dd, 1H, H-2), 4.78 (s, 1H, NHC=O), 4.22, 4.06 (2m, 2H, H-6, H-6'), 3.98 (m, 1H, αCH), 3.80 (m, 1H, H-5), 2.07, 2.04, 2.02, 2.00 (4s, 12H, 4Ac), 1.44 (s, 9H, 3 x Boc CH_3), 1.24 (m, 30H, $15CH_2$), 0.88 (t, 3H, CH_3); FAB MS $C_{37}H_{64}N_2O_{12}$ (728.91) m/z (%) 751 $[M+Na]^+$ (33), 861 $[M+Cs]^+$ (27), 629 $[M-Boc+H]^+$ (75).

Cognate preparation of 2,3,4,6-tetra-*O*-acetyl-*N*-{1-(R/S)-[(*tert*-butoxycarbonyl)amino]dodecyl}-β-D-galactopyranosylamide (**18**) from (**11**) and 2-(R/S)-[(*tert*-Butoxycarbonyl)amino]dodecanoic acid

R_F = 0.54 chloroform:methanol 10:0.2 (v/v); yield 66%; ^1H NMR δ 5.52 (d, 1H, H-4), 5.16 (m, 3H, H-1, H-2, H-3), 4.75

(br, 1H, NH), 4.21, 4.09 (2m, 4H, αCH, H-5, H-6, H-6′), 2.19, 2.06, 2.03, 1.99 (4s, 12H, 4Ac), 1.45 (s, 9H, 3 x Boc CH_3), 1.26 (m, 18H, $9CH_2$), 0.88 (t, 3H, CH_3); FAB MS $C_{31}H_{52}N_2O_{12}$ (644.75) m/z (%) 667 $[M+Na]^+$ (65), 544 $[M-Boc+H]^+$ (55), 331 (40).

Cognate preparation of 2,3,4,6-tetra-*O*-acetyl-*N*-{1-(R/S)-[(*tert*-butoxycarbonyl)amino]tetradecyl}-β-D-galactopyranosylamide (**19**) from (**11**) and 2-(R/S)-[(*tert*-Butoxycarbonyl)amino]tetradecanoic acid

R_F = 0.38 hexane:ethyl acetate 1:1 (v/v); yield 69%; ^1H NMR δ 5.53 (m, 1H, H-4), 5.25 - 5.13 (m, 3H, H-1, H-2, H-3), 4.20 - 4.11 (m, 4H, αCH, H-5, H-6, H-6′), 2.17, 2.04, 2.03, 2.00 (4s, 12H, 4Ac), 1.43 (s, 9H, 3 x Boc CH_3), 1.26 (m, 22H, $11CH_2$), 0.87 (t, 3H, CH_3); FAB MS $C_{33}H_{56}N_2O_{12}$ (672.80) m/z (%) 695 $[M+Na]^+$ (25), 573 $[M-Boc+H]^+$ (100).

Cognate preparation of 2,3,4,6-tetra-*O*-acetyl-*N*-{1-(R/S)-[(*tert*-butoxycarbonyl)amino]hexadecyl}-β-D-galactopyranosylamide (**20**) from (**11**) and 2-(R/S)-[(*tert*-Butoxycarbonyl)amino]hexadecanoic acid

R_F = 0.40 ethyl acetate; yield 66%; ^1H NMR δ 5.43 (d, 1H, H-4), 5.22 (m, 1H, H-3), 5.12 (m, 2H, H-1, H-2), 4.80 (br s, 1H, NH), 4.09 (m, 3H, αCH, H-6, H-6′), 4.02 (m, 1H, H-5), 2.17, 2.03, 1.99 (3s, 12H, 4Ac), 1.46, 1.44 (2s, 9H, 3 x Boc CH_3), 1.35 - 1.22 (m, 26H, $13CH_2$), 0.88 (t, 3H, CH_3); MALDI TOF MS $C_{35}H_{60}N_2O_{12}$ (700.86) m/z (%) 724 $[M+Na]^+$ (100), 602 $[M-Boc+H]^+$ (51).

Cognate preparation of *O*-[2′,3′,4′,6′-tetra-*O*-acetyl-α-D-glucopyranosyl(1′→4)]-2,3,6-tri-*O*-acetyl-*N*-{1-(R/S)-[(*tert*-butoxycarbonyl)amino]octadecyl}-α-D-glucopyranosylamide (**23**) from (**13**) and 2-(R/S)-[(*tert*-Butoxycarbonyl)amino]octadecanoic acid

R_F = 0.56 chloroform:methanol 10:0.3 (v/v); yield 64%; ^1H NMR δ? 5.40 - 5.22 (m, 4H), 5.05 (t, 1H), 4.86 (m, 1H), 4.77 (m, 1H), 4.39 (m, 1H), 4.22 (m, 2H), 4.02 (m, 2H),

3.94 (m, 2H), 3.78 (m, 1H), 2.12 - 1.99 (7s, 21H, 7Ac), 1.70 (m, 2H, αCH_2), 1.44, 1.43 (2s, 9H, 3 x Boc CH_3), 1.25 (m, 28H, $14CH_2$), 0.87 (t, 3H, CH_3); Anal. Calcd. for $C_{49}H_{80}N_2O_{20}$ (1017.16): C, 57.87; H, 7.87; N, 2.75. Found C, 57.72; H, 7.91; N, 2.81; FAB MS (1017.16) m/z (%) 1039 $[M+Na]^+$ (97), 918 (100).

Cognate preparation of *O*-{*O*-[2'',3'',4'',6''-tetra-*O*-acetyl-α-D-glucopyranosyl(1''→4')]-2',3',6'-tetra-*O*-acetyl-α-D-glucopyranosyl(1'→4)}-1,2,3,6-tetra-*O*-acetyl-*N*-{1-(R/S)-[(*tert*-butoxycarbonyl)amino]octadecyl}-β-D-glucopyranosylamide (**24**) from **(14)** and 2-(R/S)-[(*tert*-Butoxycarbonyl)amino]octadecanoic acid.

R_F = 0.11 chloroform:methanol 10:0.2 (v/v); yield, 53%; ^1H NMR δ ? 5.40 - 5.33 (m, 4H), 5.25 (m, 2H), 5.06 (dd, 1H), 4.90 (dd, 1H), 4.76 (m, 2H), 4.43 (m, 1H), 4.23 (m, 2H), 4.16 (d, 1H), 4.06 (dd, 1H), 3.94 (m, 5H), 3.82 (m, 1H), 2.15 - 1.99 (10s, 30H, 10Ac), 1.70 (m, 2H, βCH_2), 1.44, 1.43 (2s, 9H, 3 x Boc CH_3), 1.25 (m, 28H, $14CH_2$), 0.88 (t, 3H, CH_3); Anal. Calcd. for $C_{49}H_{80}N_2O_{20}$ (1305.41): C, 56.13; H, 7.36; N, 2.15. Found C, 56.02; H, 7.42; N, 2.19; FAB MS (1305.41) m/z (%) 1328 $[M+Na]^+$ (28), 1438 $[M+Cs]^+$ (18), 439 (10).

Example 4

2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-*N*-{1-(R/S)-[(*tert*-butoxycarbonyl)amino]-tetradecyl}-β-D-glucopyranosylamide (**21**)

Tributyl-*n*-phosphine (4.88 g, 24.2 mmol) was dissolved in abs. CH_2Cl_2 (50 ml) and added dropwise to a stirred solution of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl azide (**8**) (6.00 g, 16.1 mmol) and 2-(R/S)-[(*tert*-butoxycarbonyl)amino]tetradecanoic acid (10.2 g, 32.3 mmol) in abs. CH_2Cl_2 (100 ml) over 20 minutes. After stirring for 2 hours at room temperature, the reaction mixture was diluted with CH_2Cl_2 (100 ml) and washed with

$NaHCO_{3(sat,\ aq)}$ (2 x 100 ml). The organic phase was dried over $MgSO_4$, filtered and evaporated. The product was purified by column chromatography in chloroform:methanol 10:0.2 (v/v) to give (**21**) (8.50 g, 82%).
R_F = 0.64 hexane:ethyl acetate 1:3 (v/v);
^1H NMR δ 5.11, 5.01 (2m, 2H, H-3, H-4), 4.45 (d, 1H, H-1, $J_{1,2}$=9.5 Hz), 4.21, 4.10 (2m, 3H, αCH, H-6, H-6'), 3.81 - 3.65 (m, 2H, H-2, H-5), 2.06, 2.05, 2.00, 1.97 (3s, 12H, 4Ac), 1.43 (s, 9H, 3 x Boc CH_3), 1.25 (m, 22H, $11CH_2$), 0.86 (t, 3H, CH_3); FAB MS $C_{33}H_{57}N_3O_{11}$ (671.82) m/z (%) 694 $[M+Na]^+$ (45), 572 $[M-Boc+H]^+$ (100).

Cognate preparation of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-*N*-{1-(R/S)-[(*tert*-butoxycarbonyl)amino]-dodecyl}-β-D-glucopyranosylamide (**22**) from (**8**) and 2-(R/S)-[(*tert*-butoxycarbonyl)amino]dodecanoic acid.
R_F = 0.64 chloroform:methanol 10:0.7 (v/v); yield 76%; ^1H NMR δ 5.09 - 4.98 (m, 2H, H-3, H-4), 4.41 (d, 1H, H-1, $J_{1,2}$=9.6 Hz), 4.20 - 4.08 (m, 3H, αCH, H-6, H-6'), 3.68 (m, 2H, H-2, H-5), 2.07, 1.99, 1.96 (3s, 12H, 4Ac), 1.44 (s, 9H, 3 x Boc CH_3), 1.26 (m, 18H, $9CH_2$), 0.87 (t, 3H, CH_3); FAB MS $C_{31}H_{53}N_3O_{11}$ (643.77) m/z (%) 644 $[M+H]^+$ (40), 544 $[M-Boc+H]^+$ (100).

Example 5

N-{1-(R/S)-[(*tert*-butoxycarbonyl)amino]dodecyl}-β-D-glucopyranosylamide (**25**) from (**15**)

2,3,4,6-tetra-*O*-acetyl-*N*-{1-(R/S) -[(*tert*-butoxycarbonyl)amino]dodecyl}-β-D-glucopyranosylamide **(15)** (4.00 g, 6.182 mmol) was dissolved in abs. methanol (40 ml). Sodium methoxide was added (0.5M, 0.618 mmol) and the reaction was stirred for 3 hours. The reaction was neutralised with Amberlite H^+ ion exchange resin. The solution was then filtered and the resin washed with methanol.

R_F = 0.51 chloroform:methanol 10:2.5 (v/v); yield 87%; ^1H NMR δ 4.86 (d, 1H, H-1, $J_{1,2}$=9.3 Hz), 3.98 (m, 1H, αCH), 3.79, 3.62 (2m, 2H, H-6, H-6'), 3.37 - 3.21 (m, 4H), 1.41 (s, 9H, 3 x Boc CH_3), 1.26 (m, 18H, $9CH_2$), 0.87 (t, 3H, CH_3); FAB MS $C_{23}H_{44}N_2O_8$ (476.60) m/z (%) 477 $[M+H]^+$ (3), 499 $[M+Na]^+$ (80), 377 $[M-Boc+H]^+$ (10).

Cognate preparation of N-{1-(R/S)-[(*tert*-butoxycarbonyl)amino]dodecyl}-β-D-galactopyranosylamide (**26**) from (**18**)

R_F = 0.28 chloroform:methanol 10:2 (v/v); yield 85%; ^1H NMR δ 5.49 (d, 1H, NH), 4.87 (m, 1H, H-1), 4.10 - 3.95 (m, 1H, αCH), 3.89 (d, 1H, H-4), 3.70 - 3.51 (3m, 5H, H-2, H-3, H-5, H-6, H-6'), 1.45 (s, 9H, 3 x Boc CH_3), 1.29 (m, 18H, $9CH_2$), 0.90 (t, 3H, CH_3); FAB MS $C_{23}H_{44}N_2O_8$ (476.60) m/z (%) 499 $[M+Na]^+$ (35), 399 $[M-Boc+H]^+$ (90).

Cognate preparation of 2-acetamido-2-deoxy-*N*-{1-(R/S)-[(*tert*-butoxycarbonyl)amino]dodecyl}-β-D-glucopyranosyl amide (**27**) from (**22**)

R_F = 0.39 chloroform:methanol 10:2 (v/v); yield 87%; ^1H NMR δ, 3.86 - 3.38 (m, 8H), 1.41 (s, 9H, 3 x Boc CH_3), 1.28 - 1.21 (m, 18H, $9CH_2$), 0.86 (t, 3H, CH_3); FAB MS $C_{25}H_{47}N_3O_8$ (517.66) m/z (%) 518 $[M+H]^+$ (40), 540 $[M+Na]^+$ (50).

Example 6

N-(2-amino-(R/S)-dodecoyl)-β-D-glucopyranosylamine (**30**)

Residue (**25**) (1.34 g, 2.82 mmol) was dissolved in CH_2Cl_2:TFA 1:1 (v/v) (6 ml) and stirred at room temperature for 15 minutes. The solvent was evaporated and co-evaporated with toluene to give (**30**) (860 mg, 81%). R_F = 0.05 chloroform:methanol 10:2 (v/v); ^1H NMR δ 4.88 - 3.30 (m, 8H), 1.28 - 1.16 (m, 18H, $9CH_2$), 0.78 (t, 3H, CH_3); FAB MS $C_{18}H_{36}N_2O_6$ (376.49) m/z (%) 377 $[M+H]^+$ (10), 399 $[M+Na]^+$ (30).

Cognate preparation of *N*-(1-amino-(R/S)-dodecoyl)-β-D-galactopyranosylamine (**31**) from (**26**).

R_F = 0.05 chloroform:methanol 10:2 (v/v); yield 97%; ^1H NMR δ 4.20 - 3.24 (m, 8H), 1.38 - 1.16 (m, 18H, $9CH_2$), 0.78 (t, 3H, CH_3); FAB MS $C_{18}H_{36}N_2O_6$ (376.49) m/z (%) 399 $[M+Na]^+$ (60).

Cognate preparation of 2-acetamido-2-deoxy-*N*-(1-amino-(R/S)-dodecoyl)-β-D-glucopyranosylamine (**32**) from (**27**).

R_F = 0.05 chloroform:methanol 10:2 (v/v); yield 95%; ^1H NMR δ 7.35 (m, 1H, NH), 4.91 (m, 1H, H-1), 3.94 - 3.31 (m, 8H), 1.28 - 1.20 (m, 18H, $9CH_2$), 0.82 (t, 3H, CH_3); FAB MS $C_{20}H_{39}N_3O_6$ (417.54) m/z (%) 418 $[M+H]^+$ (3), 440 $[M+Na]^+$ (5).

Cognate preparation of *O*-[α-D-glucopyranosyl(1'→4)]-*N*-{1-amino-(R/S)-octadecoyl}-β-D-gluco-pyranosylamine (**33**)

De-*O*-protection of **23** was effected using the procedure described in experiment 5 to give **28**, which was subsequently de-*N*-protected, using the procedure described above to give **33**.

R_F = 0.31 chloroform:methanol 1:1 (v/v); yield 81%; ^1H NMR (CD_3OD) δ 5.18 - 4.96 (m, 2H), 3.88 - 3.42 (m, 12H), 1.28 (m, 30H, $15CH_2$), 0.88 (t, 3H, CH_3); Anal. Calcd. for $C_{30}H_{58}N_2O_{11}$ (622.40): C, 57.87; H, 9.32; N, 4.50. Found C, 57.82; H, 9.37; N, 4.44; FAB MS (622.40) m/z (%) 623

$[M+H]^+$ (3), 645 $[M+Na]^+$ (6), 307 (100); HRMS Calcd. for $C_{30}H_{58}N_2O_{11}$: 623.4119. Found 623.4110.

Cognate preparation of *O*-{*O*-[α-D-glucopyranosyl(1''→4')]-α-D-glucopyranosyl(1'→4)}-*N*-{1-amino-(R/S)-octadecoyl}-β-D-glucopyranosylamine (**34**)

De-*O*-protection of **24** was effected using the procedure described in experiment 5 to give **29**, which was subsequently de-*N*-protected, using the procedure described above to give **34**.

R_F = 0.39 chloroform:methanol 3:2 (v/v); yield 75%; ^1H NMR (CD_3OD) δ 5.08 (m, 3H), 3.90 - 3.37 (m, 18H), 1.29 (m, 30H, $15CH_2$), 0.89 (t, 3H, CH_3); Anal. Calcd. for $C_{36}H_{68}N_2O_{16}$ (784.46): C, 55.10; H, 8.67; N, 3.57. Found C, 55.33; H, 8.44; N, 3.63; FAB MS (784.46) m/z (%) 785 $[M+H]^+$ (50), 807 $[M+Na]^+$ (100); HRMS Calcd. for $C_{36}H_{68}N_2O_{16}Na$: 807.4467. Found 807.4460.

Example 7

Piperacillin / 2-acetamido-2-deoxy-*N*-(1-amino-(R/S)-dodecoyl)-β-D-gluco-pyranosylamine Ionic Complex (**35**)

Piperacillin (2.00 g, 3.87 mmol) and 2-acetamido-2-deoxy-*N*-(1-amino-(R/S)-dodecoyl)-β-D-glucopyranosylamine (**32**) (1.61 g, 3.87 mmol) were dissolved in 95% acetic acid. Once fully dissolved, the solution was filtered and lyophilised to give (**35**) as a white solid (3.50 g, 97%).

RP-HPLC: R_t=12.46 min. ESI MS [M (complex **35**) = 934; M^1 (glycolipid **32**) = 417] m/z (%) 935 $[M+H]^+$ (100), 418 $[M^1+H]^+$ (45).

Example 8 Preparation of glycosyl halides.

2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide (36)

Acetic anhydride (1 ml) was added to HBr in acetic acid (45%, 12 ml) and allowed to stir for 30 minutes. 1,2,3,4,6-penta-*O*-acetyl-α/β-D-galactopyranose **6** (6.00 g,

15.4 mmol) was then dissolved in a minimal quantity of absolute CH_2Cl_2, added to the solution and stirred for 2 hours. The reaction mixture was then diluted with CH_2Cl_2 (cold, -15°C, 100 ml), washed with water (3 x 300 ml) and $NaHCO_{3(sat, aq)}$ (1 x 300 ml). The organic phase was dried over $MgSO_4$, filtered and evaporated. Purification by column chromatography gave **19** (6.05 g, 96%).

R_F = 0.52 hexane:ethyl acetate 1:2 (v/v); ^1H NMR δ 6.71 (d, 1H, H-1, $J_{1,2}$=3.5 Hz), 5.52 (d, 1H, H-4), 5.42 (dd, 1H, H-3), 5.03 (dd, 1H, H-2), 4.50 (t, 1H, H-6'), 4.16 (m, 2H, H-6, H-5); FAB MS $C_{14}H_{19}BrO_9$ (411.20) m/z (%) 433, 435 $[M+Na]^+$ (17, 16), 543, 545 $[M+Cs]^+$ (67, 65), 331 $[M-Br]^+$ (100).

Cognate preparation of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (37)

R_F = 0.61 hexane:ethyl acetate 1:1 (v/v); yield 93%; ^1H NMR δ 6.52 (d, 1H, H-1, $J_{1,2}$=3.6 Hz), 5.46 (d, 1H, H-3), 5.38 (dd, 1H, H-4), 4.94 (dd, 1H, H-2), 4.44 (t, 1H, H-6'), 4.12 (m, 2H, H-6, H-5), 2.15, 2.10, 2.05, 1.97 (4s, 12H, 4Ac); FAB MS $C_{14}H_{19}BrO_9$ (411.20) m/z (%) 433, 435 $[M+Na]^+$ (34, 31), 543, 545 $[M+Cs]^+$ (71, 69), 331 $[M-Br]^+$ (80).

Cognate preparation of 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl bromide (38)

R_F = 0.35 hexane:ethyl acetate 1:1 (v/v); yield 91%; ^1H NMR δ 6.27 (d, 1H, H-1, $J_{1,2}$=1.4 Hz), 5.66 (dd, 1H, H-3), 5.35 (dd, 1H, H-2), 5.27 (m, 1H, H-4), 4.25 (m, 1H, H-6'), 4.12, 4.07 (2m, 2H, H-6, H-5), 2.17, 2.11, 2.06, 2.01 (4s, 12H, 4Ac); FAB MS $C_{14}H_{19}BrO_9$ (411.20) m/z (%) 411, 412 $[M+H]^+$ (30, 30), 433, 435 $[M+Na]^+$ (29, 29), 331 $[M-Br]^+$ (100).

Preparation of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride (39)

2-acetamido-2-deoxy-α-D-glucopyranose (15.0 g, 67.8 mmol) was suspended in acetyl chloride (65 ml) and stirred

at 45°C for 12 hours. The acetyl chloride was then removed by evaporation and co-evaporation with toluene and benzene. The product was purified by column chromatography using chloroform:ethyl acetate 10:4 (v/v) to give **39** (15.9 g, 64%).

R_F = 0.65 hexane:ethyl acetate 1:4 (v/v); ^1H NMR δ 6.17 (d, 1H, H-1, $J_{1,2}$=3.6 Hz), 5.88 (d, 1H, NH), 5.29 (t, 1H, H-3), 5.20 (m, 1H, H-4), 4.50 (m, 1H, H-2), 4.25, 4.10 (2m, 3H, H-6, H-6', H-5), 2.09, 2.03, 2.02, 1.97 (4s, 12H, 4Ac); FAB MS $C_{14}H_{20}ClNO_8$ (365.76) m/z (%) 366 $[M+H]^+$ (100), 388 $[M+Na]^+$ (75), 331 $[M-Cl]^+$ (18).

Example 9: Preparation of lipoamino acids

2-(R/S)-[(*tert*-Butoxycarbonyl)amino]dodecanoic acid (40)

Diethyl acetamidomalonate (81.3 g, 0.375 mol) was added to a stirred solution of sodium (8.40 g, 0.365 mol) in abs. ethanol (300 ml). 1-bromodecane (110 g, 0.498 mol, 105 ml) was then added to the solution. The reaction mixture was refluxed for 24 hours. After evaporation of the solvent, the oily residue was taken up in ethyl acetate (500 ml) and washed with water (1 x 500 ml) and brine (1 x 500 ml). The solution was then dried over $MgSO_4$, filtered and evaporated. The resulting oil was dissolved in concentrated hydrochloric acid (600 ml) and DMF (70 ml) and refluxed for 48 hours. On completion, the reaction mixture was poured onto ethanol:water 3:1 (750 ml). A solid product was precipitated from ammonia, filtered off and washed with ether (2 x 100 ml). The solid lipoamino acid [2-(R/S)-aminododecanoic acid] was then suspended in *tert*-butanol:water 2:3 (900 ml) and the pH corrected to 11. Di-*tert*-butyl dicarbonate (101 g, 0.463 mol) was then added to the solution, which was subsequently stirred for 48 hours. The solution was diluted with water (360 ml) and made pH 3 by addition of potassium hydrogensulphate. The product was extracted into ethyl acetate (500 ml) and was washed with brine (1 x 500 ml). The solution was then dried over

$MgSO_4$, filtered and evaporated. Re-crystallisation from acetonitrile gave **40** (96.2 g, 82%).

R_F = 0.41 hexane:ethyl acetate 4:1 (v/v); ^1H NMR δ 4.99 (s, 1H, NH), 4.30 (m, 1H, αCH), 1.42 (s, 9H, 3 x Boc CH_3), 1.20 - 1.29 (m, 18H, $9CH_2$), 0.86 (t, 3H, CH_3); FAB MS $C_{17}H_{33}O_4N$ (315.45) m/z (%) 316 $[M+H]^+$ (27), 338 $[M+Na]^+$ (95), 216 $[M-Boc+H]^+$ (68).

Cognate preparation of 2-(R/S)-[(*tert*-Butoxycarbonyl)amino]tetradecanoic acid (41)

R_F = 0.26 hexane:ethyl acetate 4:1 (v/v); yield 68%; ^1H NMR δ 5.00 (s, 1H, NH), 4.28 (m, 1H, αCH), 1.40 (s, 9H, 3 x Boc CH_3), 1.24 (m, 22H, $11CH_2$), 0.87 (t, 3H, CH_3); FAB MS $C_{19}H_{37}O_4N$ (343.50) m/z (%) 344 $[M+H]^+$ (20), 366 $[M+Na]^+$ (80), 243 $[M-Boc+H]^+$ (75).

Cognate preparation of 2-(R/S)-[(*tert*-Butoxycarbonyl)amino]hexadecanoic acid (42)

R_F = 0.41 hexane:ethyl acetate 4:1 (v/v); ^1H NMR δ 4.32 (m, 1H, αCH), 1.43 (s, 9H, 3 x Boc CH_3), 1.22 (m, 26H, $13CH_2$), 0.86 (t, 3H, CH_3); FAB MS $C_{21}H_{41}O_4N$ (371.55) m/z (%) 372 $[M+H]^+$ (27), 394 $[M+Na]^+$ (70), 272 $[M-Boc+H]^+$ (40).

Cognate preparation of 2-(R/S)-[(*tert*-Butoxycarbonyl)amino]octadecanoic acid (43)

R_F = 0.39 hexane:ethyl acetate 4:1 (v/v); ^1H NMR δ 5.01 (m, 1H, NH), 4.28 (m, 1H, αCH), 1.42 (s, 9H, 3 x Boc CH_3), 1.23 (m, 28H, $15CH_2$), 0.87 (t, 3H, CH_3); FAB MS $C_{23}H_{45}O_4N$ (399.61) m/z (%) 400 $[M+H]^+$ (37), 422 $[M+Na]^+$ (20), 300 $[M-Boc+H]^+$ (80).

Example 10 Preparation of lipoamino alcohols.

***tert*-butyl *N*-[1-(R/S)-(hydroxymethyl)tridecyl]carbamate (44)**

2-(R/S)-[(*tert*-butoxycarbonyl)amino]tetradecanoic acid **41** (1.00 g, 2.92 mmol) in abs. THF (3 ml) was added slowly dropwise to BH_3-THF complex (1.0M, 5.8 ml, 5.80

mmol) at 0°C. After stirring for 2 hours, the reaction mixture was quenched with 10% acetic acid in methanol (v/v) and evaporated. The residue was taken up in CH_2Cl_2 (10 ml) and washed with 1M $KHSO_{4(aq)}$ (1 x 20 ml) and brine (2 x 20 ml). The solution was then dried over $MgSO_4$, filtered and evaporated. Purification by column chromatography gave **44** (821 mg, 86%).

R_F = 0.82 chloroform:methanol 10:1 (v/v); ^1H NMR δ 3.72 - 3.48 (m, 3H, αCH, CH_2), 1.40 (s, 9H, 3□x Boc CH_3), 1.25 (m, 22H, 11CH_2), 0.86 (t, 3H, CH_3); FAB MS $C_{19}H_{39}NO_3$ (329.52) m/z (%) 330 $[M+H]^+$ (6), 352 $[M+Na]^+$ (10), 462 $[M+Cs]^+$ (8), 230 $[M-Boc+H]^+$ (100).

Cognate preparation of *tert*-butyl *N*-[1-(R/S)-(hydroxymethyl) pentadecyl]carbamate (45)

Procedure as for **44**, Method C (using **42** in place of **41**).

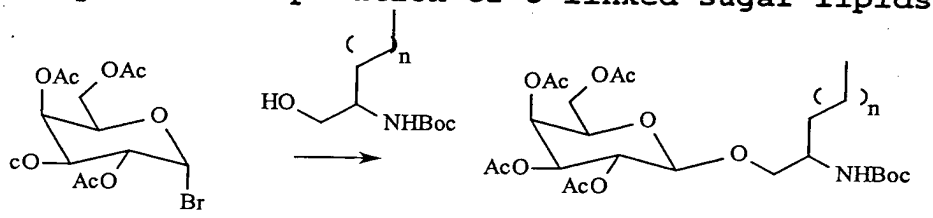
R_F = 0.72 chloroform:methanol 10:0.7 (v/v); yield 82%; ^1H NMR δ 3.69 - 3.45 (m, 2H, αCH, CH_{2a}), 2.97 (m, 1H, CH_{2b}), 1.41 (s, 9H, 3?x Boc CH_3), 1.25 (m, 18H, 13CH_2), 0.88 (t, 3H, CH_3); FAB MS $C_{21}H_{43}NO_3$ (357.32) m/z (%) 380 $[M+Na]^+$ (15), 258 $[M-Boc+H]^+$ (100).

Cognate preparation of *tert*-butyl *N*-[1-(R/S)-(hydroxymethyl) undecyl]carbamate (46)

Procedure as for **44** (using **40** in place of **41**).

R_F = 0.50 hexane:ethyl acetate 4:1 (v/v); yield 87%; ^1H NMR δ 3.65 - 3.48 (m, 3H, αCH, CH_2), 1.43 (s, 9H, 3?x Boc CH_3), 1.24 (m, 18H, 9CH_2), 0.86 (t, 3H, CH_3); FAB MS $C_{17}H_{35}NO_3$ (301.46) m/z (%) 302 $[M+H]^+$ (15), 324 $[M+Na]^+$ (5), 434 $[M+Cs]^+$ (10), 202 $[M-Boc+H]^+$ (95).

Example 11: Preparation of O-linked sugar-lipids



Example 13

2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide **36** (10 gm) is dissolved in anhydrous dichloroethane (150 mL) and to this solution is added freshly activated 4A molecular sieves (10 gm). The resultant solution is stirred under nitrogen and *tert*-butyl *N*-[1-(R/S)-(hydroxymethyl) undecyl]carbamate (9a) (9.5 gm, 1.3 eq) is added. Finally, silver trifluoromethanesulfonate (10 gm) is added and the reaction mixture stirred at room temperature for 2 hours. After this time the solution is filtered through a pad of celite, and the solution extracted with 2 times 100 mL of saturated sodium chloride solution then dried over magnesium sulfate. The solution is filtered, evaporated to dryness and chromatographed on silica (hexane:ethyl acetate 2:1) to yield the β glycoside as the major product.

Reaction with other aminoalcohols and other glycosyl halides proceeds in a similar manner, with the exception of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride (**39**), which did not yield the desired product. An alternative procedure for this material via the trichloroacetimidate is described below.

1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α/β-D-glucopyranose (47)

2,2,2-Trichloroethoxycarbonyl chloride (Troc-Cl) (12.7 g, 59.9 mmol) was added dropwise at room temperature to a vigorously stirred solution of α-D-glucosamine hydrochloride and $NaHCO_3$ (12.6 g, 150 mmol) in water (150 ml). The solution was stirred for 1 hour. The reaction mixture was then neutralised with 1M HCl (50 ml) and evaporated. The residue was dissolved in pyridine (50 ml)

and acetic anhydride (25 ml) and was stirred for 12 hours. Following evaporation, the residue dissolved in CH_2Cl_2 (200 ml) and was washed with 1M $HCl_{(aq)}$ (1 x 200 ml), water (1 x 200 ml) and sat. $NaHCO_3$ (1 x 200 ml). The organic phase was dried over $MgSO_4$, filtered and evaporated to give **47** (22.6 g, 72%) as white foamy crystalline material.

R_F = 0.31 hexane:ethyl acetate 1:1 (v/v); ^1H NMR δ 6.22 (d, 1H, NH), 5.27 - 5.16 (m, 3H, H-1, H-3, H-4), 4.80, 4.60 (2d, 2H, $Cl_3CC\underline{H}_2$), 4.27 - 4.10 (m, 2H, H-2, H-6), 4.06 - 3.90 (m, 2H, H-5, H-6'), 2.19, 2.10, 2.03, 2.02 (4s, 12H, 4Ac); FAB MS $C_{17}H_{22}Cl_3NO_{11}$ (522.71) m/z (%) 546 $[M+Na]^+$ (18), 462 $[M-OAc]^+$ (43).

3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α/β-D-glucopyranose (48)

1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α/β-D-gluco-pyranose **47** (3.10 g, 5.99 mmol) and hydrazine acetate (660 mg, 7.17 mmol) were stirred in abs. DMF (30 ml) at room temperature for 40 minutes. Following evaporation, the residue dissolved in CH_2Cl_2 (80 ml) and was washed with brine (1 x 50 ml) and water (1 x 30 ml). The solution was dried over $MgSO_4$, filtered and evaporated to give **48** (2.80 g, crude), which was used in the next reaction without further purification.

R_F = 0.25 hexane:ethyl acetate 1:1 (v/v); ^1H NMR δ 5.35 - 5.31 (m, 2H, H-1, H-4), 5.12 (t, 1H, H-3), 4.80, 4.63 (2d, 2H, $Cl_3CC\underline{H}_2$), 4.23 - 4.19 (m, 2H, H-2, H-6), 4.15 - 4.00 (m, 2H, H-5, H-6'), 2.09, 2.03, 2.00 (3s, 9H, 3Ac); FAB MS $C_{15}H_{20}Cl_3NO_{10}$ (480.68) m/z (%) 502 $[M+Na]^+$ (17), 464 $[M-OH]^+$ (48), 302 $[M-troc+H]^+$ (93).

***O*-[3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α/β-D-glucopyranosyl] trichloroacetimidate (49)**

Sodium hydride (0.32 g, 8.10 mmol) was added to a mixture of 3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α/β-D-glucopyranose **48** (2.80

g, 5.83 mmol), trichloroacetonitrile (5.05 g, 34.9 mmol) and molecular sieves (500 mg) at 0°C. The reaction was then stirred for 2 hours at room temperature. The solution was subsequently filtered through a celite pad, evaporated and the residue was purified by column chromatography in hexane:ethyl acetate 6:4 (v/v) to give **49** (1.70 g, 47%).

R_F = 0.46 hexane:ethyl acetate 1:1 (v/v); ^{1}H NMR δ 6.42 (m, 1H, H-1, $J_{1,2}$=3.2 Hz), 5.35 - 5.20 (m, 3H, H-3, H-4, NH), 4.70 (d, 2H, $Cl_3CC\underline{H}_2$), 4.29 - 4.25 (m, 2H, H-2, H-6), 4.15 - 4.10 (m, 2H, H-5, H-6'), 2.09, 2.05, 2.03 (3s, 9H, 3Ac); FAB MS $C_{17}H_{20}Cl_6N_2O_{10}$ (625.06) m/z (%) 648 $[M+Na]^+$ (8), 461 $[M-OC(NH)CCl_3]^+$ (44), 301 $[M-troc+H]^+$ (100).

***tert*-Butyl 1-{[3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonyl-amino)-β-D-glucopyranosyloxy]methyl}-(R/S)-undecylcarbamate (50)**

O-[3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-gluco-pyranosyl] trichloroacetimidate **49** (125 mg, 0.20 mmol), *tert*-butyl *N*-[1-(R/S)-(hydroxymethyl)undecyl]carbamate **46** (45.0 mg, 0.150 mmol) and molecular sieves (200 mg) were stirred in abs. CH_2Cl_2 (5 ml) for 15 minutes. Boron trifluoride etherate (64.0 mg, 0.451 mmol) in abs. CH_2Cl_2 (3 ml) was added dropwise at 0°C over 20 minutes. The mixture was stirred for 2 hours at room temperature. The reaction mixture was then diluted with CH_2Cl_2 (10 ml) and filtered through a Celite pad. The solution was washed with $NaHCO_{3(sat,aq)}$ (1 x 10 ml) and water (1 x 10 ml). The organic layer was dried over $MgSO_4$, filtered and evaporated. The residue was purified by column chromatography using hexane:ethyl acetate 6:4 (v/v) to give **50** (40.0 mg, 35%).

R_F = 0.35 hexane:ethyl acetate 1:1 (v/v); ^{1}H NMR δ 5.28 - 5.21 (m, 2H, H-3, H-4), 4.79, 4.63 (2m, 2H, $Cl_3CC\underline{H}_2$), 4.56 (d, 1H, H-1, $J_{1,2}$=8.2 Hz), 4.25, 4.14 (2m, 2H, H-6, H-6'), 3.82 (m, 1H, H-2), 3.70 - 3.55 (m, 4H, H-5, αCH, CH_2), 2.16, 2.08, 2.02 (3s, 9H, 3Ac), 1.44 (s, 9H, 3 x Boc CH_3), 1.28 - 1.23 (m, 18H, $9CH_2$), 0.87 (t, 3H, CH_3);

FAB MS $C_{32}H_{53}Cl_3N_2O_{12}$ (764.13) m/z (%) 787 $[M+Na]^+$ (100), 462 $[M-lipid]^+$ (75), 663 $[M-Boc+H]^+$ (70).

***tert*-Butyl 1-[(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyloxy)-methyl]-(R/S)-undecylcarbamate (51)**

tert-Butyl 1-{[3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonyl-amino)-β-D-glucopyranosyloxy]methyl}-(R/S)-undecylcarbamate **50** (27.0 mg, 0.0353 mmol) was dissolved in acetic anhydride (1 ml) into which activated zinc powder (4.6 mg, 0.0706 mmol) had been added. The reaction was stirred for 6 hours, after which it was filtered and evaporated (and co-evaporated with benzene and toluene). The residue was purified by column chromatography to give **51** (11 mg, 49%).

R_F = 0.17 hexane:ethyl acetate 1:1 (v/v); ^1H NMR δ 5.24 - 5.16 (m, 2H, H-3, H-4), 4.51 (d, 1H, H-1, $J_{1,2}$=8.5 Hz), 4.27, 4.11 (2m, 2H, H-6, H-6'), 3.72 (m, 1H, H-2), 3.71 - 3.57 (m, 4H, H-5, αCH, CH_2), 2.16, 2.08, 2.02, 1.96 (4s, 12H, 4Ac), 1.43 (s, 9H, 3 x Boc CH_3), 1.29 - 1.24 (m, 18H, $9CH_2$), 0.87 (t, 3H, CH_3); FAB MS $C_{31}H_{54}N_2O_{11}$ (630.77) m/z (%) 653 $[M+Na]^+$ (60), 531 $[M-Boc+H]^+$ (90).

Example 12 Preparation of glycosyl isothiocyanates

2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl isothiocyanate (52)

Potassium thiocyanate (2.81 g, 28.7 mmol), tetrabutylammonium hydrogen sulphate (1.22 g, 3.59 mmol) and molecular sieves (6.00 g) were stirred in absolute acetonitrile (500 ml) for 30 minutes. 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide **37** (5.90 g, 14.4 mmol) was then dissolved in acetonitrile, added to the reaction flask and refluxed for 90 minutes. The solution was then allowed to cool, filtered through a celite pad and concentrated. Purification by column chromatography in hexane:ethyl acetate 2:1 (v/v) to give **52** (4.26 g, 76%).

R_F = 0.29 hexane:ethyl acetate 3:2 (v/v); ^1H NMR δ 5.20 (t, 1H, H-2), 5.09 (m, 2H, H-3, H-4), 5.02 (d, 1H, H-1, $J_{1,2}$=8.7 Hz), 4.24, 4.14 (2m, 2H, H-6, H-6'), 3.74 (m, 1H, H-5), 2.09, 2.01, 2.00 (3s, 12H, 4Ac); ^{13}C NMR δ 170.6, 170.1, 169.1, 168.9, 144.3, 83.5, 74.1, 72.5, 71.9, 61.8, 61.5, 20.6, 20.5, 20.5, 20.4; FAB MS $C_{15}H_{19}NO_9S$ (389.38) m/z (%) 412 $[M+Na]^+$ (8), 522 $[M+Cs]^+$ (25), 331 $[M-NCS]^+$ (100).

Cognate preparation of 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl isothiocyanate (53)

R_F = 0.38 hexane:ethyl acetate 3:2 (v/v); yield 79%; ^1H NMR δ 5.39 (d, 1H, H-4), 5.28 (m, 1H, H-2), 4.99 (dd, 1H, H-3), 4.96 (m, 1H, H-1, $J_{1,2}$=8.9 Hz), 4.12 (m, 2H, H-6, H-6'), 3.95 (m, 1H, H-5), 2.16, 2.10, 2.04, 1.98 (4s, 12H, 4Ac); FAB MS $C_{15}H_{19}NO_9S$ (389.38) m/z (%) 412 $[M+Na]^+$ (5), 522 $[M+Cs]^+$ (50), 331 $[M-NCS]^+$ (100).

Cognate preparation of 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl isothiocyanate (54)

R_F = 0.40 hexane:ethyl acetate 1:1 (v/v); yield 84%; ^1H NMR δ 5.55 (d, 1H, H-1, $J_{1,2}$=2.0 Hz), 5.32 (m, 1H, H-2), 5.27 (m, 2H, H-3, H-4), 4.27, 4.14 (2m, 2H, H-6, H-6'), 4.08 (m, 1H, H-5), 2.17, 2.10, 2.06, 2.01 (4s, 12H, 4Ac); ^{13}C NMR δ 170.7, 170.4, 169.9, 169.8, 144.1, 82.8, 71.6, 69.7, 68.3, 65.4, 61.6, 20.7, 20.6, 20.5, 14.2; FAB MS $C_{15}H_{19}NO_9S$ (389.38) m/z (%) 412 $[M+Na]^+$ (5), 522 $[M+Cs]^+$ (70), 331 $[M-NCS]^+$ (100).

Cognate preparation of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl isothiocyanate (55)

Purification by column chromatography in hexane:ethyl acetate 3:2 (v/v) to give **55** (1.09 g, 74%).

R_F = 0.38 hexane:ethyl acetate 3:1 (v/v); ^1H NMR δ 5.94 (d, 1H, NH), 5.24 (t, 1H, H-3), 5.24 (d, 1H, H-1, $J_{1,2}$=9.6 Hz), 5.06 (t, 1H, H-4), 4.21, 4.11 (2m, 2H, H-

6, H-6'), 3.99 (m, 1H, H-2), 3.75 (m, 1H, H-5), 2.09 (s, 3H, NAc), 2.04, 2.02, 2.00 (3s, 9H, 3OAc); ^{13}C NMR δ 170.7, 170.6, 169.5, 169.2, 143.2, 83.9, 73.9, 71.8, 68.0, 61.7, 56.0, 23.2, 20.7, 20.6, 20.5; FAB MS $C_{15}H_{20}N_2O_8S$ (388.39) m/z (%) 411 $[M+Na]^+$ (20), 521 $[M+Cs]^+$ (65), 330 $[M-NCS]^+$ (100).

Methyl 5-acetamido-3,5-dideoxy-β-D-*glycero*-D-*galacto*-2-nonulo-pyranosonate (56)

5-Acetamido-3,5-dideoxy-α/β-D-*glycero*-D-*galacto*-2-nonulopyranosonic acid (2.00 g, 6.46 mmol) was suspended in absolute methanol (60 ml) with ion exchange resin and stirred for 72 hours. The resin was subsequently filtered off and washed with methanol. The solution was concentrated and purified by column chromatography to give **56** (1.94 g, 93%).

R_F = 0.60 chloroform:methanol:water 5:6:2 (v/v/v); ^1H NMR δ 4.00 - 3.94 (m, 2H, H-4, H-6), 3.83 (t, 1H, H-5), 3.76 (s, 3H, OCH_3), 3.74 (dd, 1H, H-9'), 3.63 (dd, 1H, H-8), 3.53 (dd, 1H, H-9), 3.46 (d, 1H, H-7), 2.22 (dd, 1H, H-3_{eq}), 1.82 (dd, 1H, H-3_{ax}); FAB MS $C_{12}H_{21}NO_9$ (323.29) m/z (%) 324 $[M+H]^+$ (5), 346 $[M+Na]^+$ (100).

Methyl 5-acetamido-2,4,7,8,9-penta-*O*-acetyl-3,5-dideoxy-α/β-D-*glycero*-D-*galacto*-2-nonulo-pyranosonate (57)

Methyl 5-acetamido-3,5-dideoxy-β-D-*glycero*-D-*galacto*-2-nonulo-pyranosonate **56** (1.94 g, 6.01 mmol) was dissolved in pyridine (22.6 ml) and acetic anhydride (25.6 ml) and stirred overnight. The pyridine was evaporated and the residue co-evaporated with toluene and benzene. Purification by column chromatography gave **57α** (570 mg, 18%) and **57β** (1.58 g, 49%).

57α : R_F = 0.40 ethyl acetate:methanol 10:0.5 (v/v); ^1H NMR δ 5.36 (dd, 2H, NH, H-7), 5.19 (dd, 1H, H-8), 5.04 - 4.99 (m, 1H, H-4), 4.68 (dd, 1H, H-6), 4.36 (dd, 1H, H-9'), 4.16 (m, 1H, H-5), 4.06 (dd, 1H, H-9), 3.76 (s, 3H, OCH_3),

2.56 (dd, 1H, H-3_{eq}), 2.07 (dd, 1H, H-3_{ax}), 2.12, 2.09, 2.02, 1.89 (4s, 18H, 6Ac); FAB MS $C_{22}H_{31}NO_{14}$ (533.48) m/z (%) 534 $[M+H]^+$ (5), 556 $[M+Na]^+$ (37), 414 (100).

57β : R_F = 0.30 ethyl acetate:methanol 10:0.5 (v/v); ^1H NMR δ 5.37 (dd, 1H, H-7), 5.31 - 5.22 (m, 2H, H-4, NH), 5.06 (dd, 1H, H-8), 4.49 (dd, 1H, H-9'), 4.15 - 4.07 (m, 3H, H-5, H-6, H-9), 3.76 (s, 3H, OCH_3), 2.55 (dd, 1H, H-3_{eq}), 2.14 (dd, 1H, H-3_{ax}), 2.16, 2.08, 2.04, 1.89 (4s, 18H, 6Ac); FAB MS $C_{22}H_{31}NO_{14}$ (533.48) m/z (%) 534 $[M+H]^+$ (2), 556 $[M+Na]^+$ (38), 414 (100).

Methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-2-chloro-3,5-dideoxy-β-D-*glycero*-D-*galacto*-2-nonulo-pyranosonate (58)

HCl gas was bubbled through acetyl chloride (150 ml) for 15 minutes at -15°C to form a saturated solution. Methyl 5-acetamido-2,4,7,8,9-penta-*O*-acetyl-3,5-dideoxy-α/β-D-*glycero*-D-*galacto*-2-nonulo-pyranosonate **57** (700 mg, 1.31 mmol) was added to the solution, which was stirred for 24 hours. The acetyl chloride was evaporated and the residue co-evaporated with toluene and benzene. Purification by column chromatography using ethyl acetate gave **58** (582 mg, 87%).

R_F = 0.5 ethyl acetate:methanol 10:0.5 (v/v); ^1H NMR δ 5.51 (d, 1H, NH), 5.47 (dd, 1H, H-7), 5.38 (m, 1H, H-4), 5.16 (m, 1H, H-8), 4.43 (dd, 1H, H-9'), 4.36 (dd, 1H, H-6), 4.21 (m, 1H, H-5), 4.08 (m, 1H, H-9), 3.87 (s, 3H, OCH_3), 2.76 (dd, 1H, H-3_{eq}), 2.27 (dd, 1H, H-3_{ax}), 2.12, 2.09, 2.05, 1.90 (4s, 15H, 5Ac); FAB MS $C_{20}H_{28}ClNO_{12}$ (509.89) m/z (%) 532 $[M+Na]^+$ (47), 496 (100).

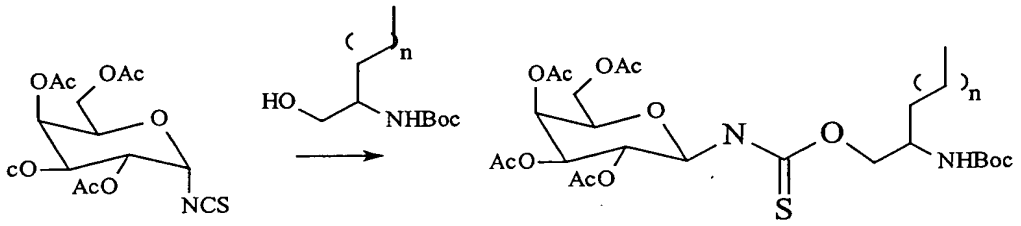
Methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-2-isothiocyanato-3,5-dideoxy-α-D-*glycero*-D-*galacto*-2-nonulopyranosonate (59)

Potassium thiocyanate (1.10 g, 11.3 mmol), tetrabutylammonium hydrogen sulphate (478 mg, 1.41 mmol) and molecular sieves (3.00 g) were stirred in absolute acetonitrile (300 ml) for 30 minutes. Methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-2-chloro-3,5-dideoxy-β-D-*glycero*-D-

galacto-2-nonulopyranosonate **58** (2.86 g, 5.63 mmol) was then dissolved in acetonitrile, added to the reaction flask and refluxed for 1 hour. The solution was then allowed to cool, filtered through a celite pad and concentrated. Purification by column chromatography gave **59** (2.01 g, 67%).

R_F = 0.21 chloroform:methanol 10:1 (v/v);
^{1}H NMR δ.45 (d, 1H, NH), 5.42 (dd, 1H, H-7, $J_{7,8}$=7.3 Hz), 5.22 (m, 1H), 5.17 (m, 1H), 4.37 (dd, 1H), 4.16 (m, 2H), 4.05 (m, 1H), 3.89 (s, 3H, $COOCH_3$), 2.48 (dd, 1H, H-3_{eq}), 2.23 (dd, 1H, H-3_{ax}), 2.10, 2.06, 2.03, 1.89 (4s, 15H, 5Ac);
^{13}C NMR δ 170.8, 170.5, 170.3, 170.0, 169.9, 169.7, 145.4, 107.9, 89.5, 76.8, 76.5, 73.5, 70.6, 69.7, 68.8, 68.5, 67.9, 67.8, 67.5, 67.0, 62.1, 61.9, 59.1, 53.9, 49.2, 48.9, 46.8, 38.9, 38.3, 24.2, 23.1, 20.9, 20.7, 19.6, 13.9; FAB MS $C_{21}H_{28}N_2O_{12}S$ (532.52) m/z (%) 533 $[M+H]^+$ (20), 555 $[M+Na]^+$ (60), 571 $[M+K]^+$ (100), 665 $[M+Cs]^+$ (70).

Example 13: Reaction of glycosyl isothiocyanates with alcohols to form thiocarbamate linkages



Example 15

2,3,4,6-tetra-*O*-acetyl-*N*-[({2-(R/S)-[(*tert*-butoxycarbonyl)amino]dodecyl}oxy)-carbonothioyl]-β-D-glucopyranosylamine (60)

2,3,4,6-tetra-*O*-cetyl-β-D-glucopyranosyl isothiocyanate **52** (1.00 g, 2.57 mmol), *tert*-butyl *N*-[1-(R/S)-(hydroxymethyl)undecyl]carbamate **46** (967 mg, 3.21 mmol) and triethylamine (130 mg, 1.29 mmol) were dissolved in abs. toluene (10 ml) and stirred under reflux for 12

hours. Following evaporation, the residue was purified by column chromatography in hexane:ethyl acetate 2:1 to give **60** (1.36 g, 77%).

R_F = 0.69 chloroform:methanol 10:2 (v/v); ^1H NMR δ 7.02 (d, 1H, NH), 5.54, 5.32, 5.05, 4.96 (4m, 4H, H-1, H-2, H-3, H-4), 4.37 (m, 1H, αCH), 4.28 (m, 1H, H-6), 4.09 (m, 3H, CH_2, H-6'), 3.81 (d, 1H, H-5), 2.05, 2.01, 2.00, 1.99 (4s, 12H, 4Ac), 1.41 (s, 9H, 3 x Boc CH_3), 1.28 - 1.21 (m, 18H, $9CH_2$), 0.85 (t, 3H, CH_3); ^{13}C NMR δ 170.6, 170.4, 169.9, 169.4, 155.3, 83.2, 81.9, 73.7, 72.7, 70.5, 69.8, 68.3, 67.6, 65.8, 61.6, 61.2, 60.2, 52.9, 49.6, 31.8 - 13.9 ; FAB MS $C_{34}H_{54}N_2O_{12}S$ (690.84) m/z (%) 713 $[M+Na]^+$ (25), 823 $[M+Cs]^+$ (100), 591 $[M-Boc+H]^+$ (40).

Cognate preparation of 2,3,4,6-tetra-*O*-acetyl-*N*-[({2-(R/S)-[(*tert*-butoxycarbonyl)amino]tetradecyl}oxy)-carbonothioyl]-β-D-glucopyranosylamine (61)

R_F = 0.29 chloroform:methanol 10:0.2 (v/v); yield 72%; ^1H NMR δ 7.05 (d, 1H, NH), 5.53 - 4.99 (2m, 4H, H-1, H-2, H-3, H-4), 4.34 (m, 1H, αCH), 4.28 - 4.06 (m, 4H, H-6, H-6', CH_2,), 3.79 (d, 1H, H-5), 2.07, 2.03, 2.02, 1.99 (4s, 12H, 4Ac), 1.43 (s, 9H, 3 x Boc CH_3), 1.25 (m, 22H, $11CH_2$), 0.87 (t, 3H, CH_3); FAB MS $C_{36}H_{58}N_2O_{12}S$ (718.90) m/z (%) 719 $[M+H]^+$ (10), 851 $[M+Cs]^+$ (50), 619 $[M-Boc+H]^+$ (70).

Example 14: Preparation of aminomethyl lipidic amines.

***tert*-butyl *N*-[1-(R/S)-(iodomethyl)undecyl]carbamate (62)**

Trimethylphosphine (1.0M, 1.33 mmol) was added dropwise to a stirred solution of (azodicarbonyl)dipiperidine [ADDP] (336 mg, 1.33 mmol) in abs. THF (25 ml) at 0°C. After 30 minutes, iodomethane (189 mg, 1.33 mmol) and *tert*-butyl *N*-[1-(R/S)-(hydroxymethyl)undecyl]carbamate **46** (200 mg, 0.664 mmol) were added to the solution, which was subsequently stirred for 4 hours at room temperature. The precipitate was then filtered off and the solution evaporated to dryness. The

residue was dissolved in ethyl acetate and the remaining hydrazide was precipitated from hexane and removed by filtration. Following evaporation, the residue was taken up in CH_2Cl_2 (50 ml), washed with water (2 x 25 ml) and with $NaHCO_{3(sat,aq)}$ (1 x 25 ml), dried with $MgSO_4$, filtered and evaporated. The residue was purified by column chromatography in hexane:ethyl acetate 4:1 (v/v) to give **62** (176 mg, 64%).

R_F = 0.79 hexane:ethyl acetate 1:1 (v/v); ^1H NMR δ 4.47 (d, 1H, NH), 3.24 (m, 1H, αCH), 2.15, 1.84 (2d, 2H, CH_2I), 1.40 (s, 9H, 3 x Boc CH_3), 1.23 (m, 18H, $9CH_2$), 0.83 (t, 3H, CH_3); ^{13}C NMR δ 155.1, 80.8, 49.6, 38.2 - 22.6, 15.1, 14.0; FAB MS $C_{17}H_{34}INO_2$ (411.36) m/z (%) 410 $[M-H]^+$ (100), 434 $[M+Na]^+$ (30), 544 $[M+Cs]^+$ (85), 340 $[M-Boc+H]^+$ (100).

***tert*-butyl *N*-[1-(R/S)-(azidomethyl)undecyl]carbamate (63)**

tert-butyl *N*-[1-(R/S)-(iodomethyl)undecyl]carbamate **62** (250 mg, 0.608 mmol) was dissolved in abs. DMF (10 ml). Sodium azide (79.0 mg, 1.22 mmol) was added to the solution, which was subsequently stirred at 110°C for 12 hours. Following evaporation, the residue was taken up in CH_2Cl_2 (50 ml) and was washed with $NaHCO_{3(sat, aq)}$ (1 x 50 ml). The organic phase was dried over $MgSO_4$, filtered and evaporated. The residue was purified by column chromatography in hexane:ether 10:1 (v/v) to give **63** (100 mg, 54%).

R_F = 0.46 hexane:ethyl acetate 5:1 (v/v); ^1H NMR δ 3.61 (m, 1H, αCH), 3.46 - 3.39 (m, 2H, CH_2), 1.43 (s, 9H, 3 x Boc CH_3), 1.25 (m, 18H, $9CH_2$), 0.87 (t, 3H, CH_3); ESI MS $C_{17}H_{34}N_4O_2$ (326.48) m/z (%) 327 $[M+H]^+$ (100), 349 $[M+Na]^+$ (15), 227 $[M-Boc+H]^+$ (20).

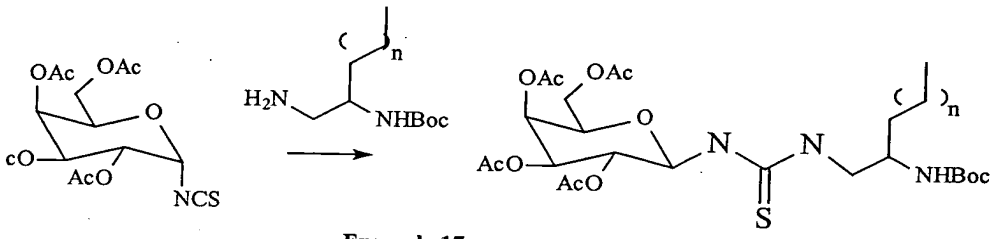
***tert*-butyl *N*-[1-(R/S)-(aminomethyl)undecyl]carbamate (64)**

Palladium catalyst (10% on carbon, 10.0 mg) was added in one portion to a solution of *tert*-butyl *N*-[1-(azidomethyl)undecyl]carbamate **63** (100 mg, 0.282 mmol) in

abs. methanol (5 ml) under a hydrogen atmosphere. The solution was allowed to stir for 12 hours. The catalyst was subsequently filtered off, and the solvent evaporated to give **64** (78 mg, 84%).

R_F = 0.59 hexane:ethyl acetate 1:1 (v/v); ^{1}H NMR δ 4.92 (d, 1H, NH), 3.74 (m, 1H, αCH), 3.05 (m, 2H, CH_2), 1.45 (s, 9H, 3 x Boc CH_3), 1.25 (m, 18H, $9CH_2$), 0.88 (t, 3H, CH_3); FAB MS $C_{17}H_{36}N_2O_2$ (300.48) m/z (%) 301 $[M+H]^+$ (55), 323 $[M+Na]^+$ (20), 201 $[M-Boc+H]^+$ (85).

Example 15: Reaction of glycosyl isothiocyanates with amines to form thiourea linkages



Example 17

2,3,4,6-tetra-*O*-acetyl-*N*-[({2-(R/S)-[(*tert*-butoxycarbonyl)amino]dodecyl}amino)-carbonothioyl]-β-D-glucopyranosylamine (65)

2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl isothiocyanate **37** (25.0 mg, 0.0617 mmol), *tert*-butyl *N*-[1-(R/S)-(aminomethyl)undecyl]carbamate (27.8 mg, 0.0927 mmol) and triethylamine (12.5 mg, 0.0124 mmol) were dissolved in abs. CH_2Cl_2 (5 ml) and stirred at room temperature for 1 hour. Following evaporation, the residue was purified by column chromatography to give **65** (42.0 mg, 94%)

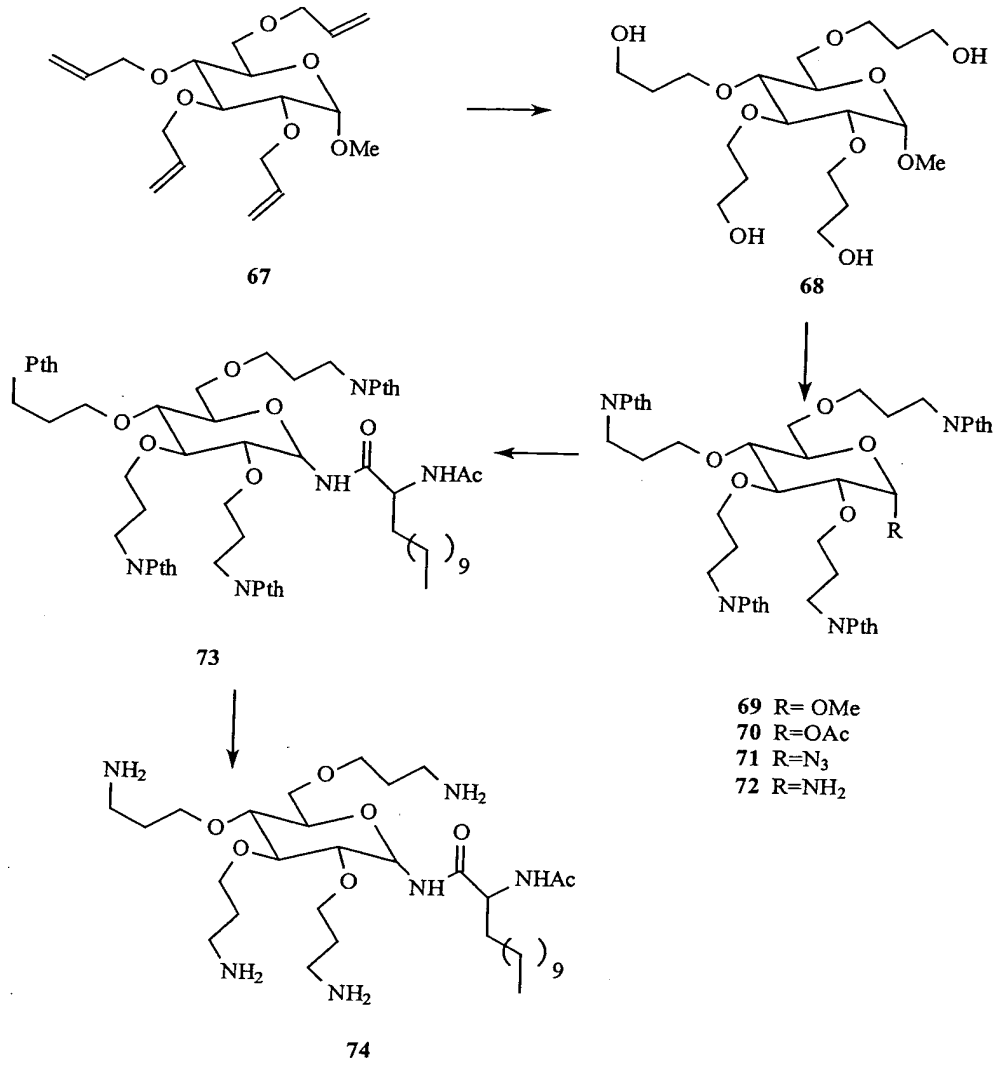
R_F = 0.39 chloroform:methanol 10:0.2 (v/v); ^{1}H NMR δ 5.11 - 4.99 (m, 3H, H-1, H-3, H-4), 4.23, 4.10 (2m, 2H, H-6, H-6'), 3.87 - 3.61 (m, 3H, H-2, H-5, αCH), 2.09, 2.01, 2.00, 1.96 (4s, 12H, 4Ac), 1.43 (s, 9H, 3 x Boc CH_3), 1.24 (m, 18H, $9CH_2$), 0.88 (t, 3H, CH_3); FAB MS $C_{32}H_{55}N_3O_{11}S$ (689.86) m/z (%) 690 $[M+H]^+$ (10), 712 $[M+Na]^+$ (30), 590 $[M-Boc+H]^+$ (100).

Cognate preparation of 2,3,4,6-tetra-*O*-acetyl-*N*-[({2-(R/S)-[(*tert*-butoxycarbonyl)amino]tetradecyl}-amino)carbonothioyl]-β-D-glucopyranosylamine (66)

Procedure as for **65**

R_F = 0.41 chloroform:methanol 10:0.2 (v/v); yield 85%; ^{1}H NMR δ 5.16 – 4.96 (m, 3H), 4.28, 4.11 (2m, 2H, H-6, H-6'), 3.84 - 3.58 (m, 3H, H-2, H-5, αCH), 2.11, 2.06, 2.04, 2.00 (4s, 12H, 4Ac), 1.44 (s, 9H, 3 x Boc CH_3), 1.25 (m, 22H, 11CH_2), 0.84 (t, 3H, CH_3); FAB MS $C_{34}H_{59}N_3O_{11}S$ (717.91) m/z (%) 718 $[M+H]^+$ (40), 618 $[M-Boc+H]^+$ (85).

Example 16: Multiple charged lipid-sugar delivery systems



67 **68**

73

69 R= OMe
70 R=OAc
71 R=N_3
72 R=NH_2

74

Compound 67 is readily prepared from commercially-available starting materials by known literature methods.

Methyl 2,3,4,6-tetra-O-(3-hydroxy-propyl)-α-D-glucopyranoside (**68**).

To a solution of **67** (1.03 g, 2.9 mmol) in dry THF (25 mL) 9-BBN (0.5M solution in THF; 70 mL, 35 mmol) was added under nitrogen and the reaction was stirred at reflux for 6 h. Then the excess of 9-BBN was destroyed by dropwise addition of water (3.0 mL) at 0 °C. The hydroboration

mixture was oxidized by adding 3M aq Na Acetate (36 mL) and 30% H_2O_2 (36 mL) slowly at 0 °C followed by stirring overnight at room temperature. The aqueous phase was saturated with K_2CO_3 and the THF phase was separated. The aqueous phase was extracted with THF (2x50 mL). The combined THF layers were dried over $MgSO_4$, filtered, and concentrated. The oily residue was purified by column chromatography (9:1→8:2 $CHCl_3$-MeOH) to yield a colorless oil (0.86 g, 70%; R_f 0.26 $CHCl_3$-MeOH; 8:2): MS(FAB): 449 $(M+Na)^+$, 427 $(M+H)^+$; ^1H NMR (500 MHz, $CDCl_3$): δ 1.77-1.82 (m, 8H, 4 $OCH_2CH_2CH_2OH$), 3.24 (dd, 1H, $J_{4,5}$ 9.2 Hz, H-4), 3.28 (dd, 1H, H-2), 3.38 (s, 3H, OCH_3), 3.48 (1H, t, $J_{3,4}$ 9.5 Hz, H-3), 3.52-3.74 (m, 16H, 4 $OCH_2CH_2CH_2OH$), 3.80 (m, 1H, H-6), 3.82-3.87 (m, 2H, H-5, H-6'), 4.80 (1H, d, $J_{1,2}$ 3.5 Hz, H-1). Anal. Calcd for $C_{19}H_{38}O_{10}$: C, 53.51; H, 9.00. Found: C, 53.60; H, 8.72

Methyl-2,3,4,6-tetra-O-3-phthalimidopropyl-α-D-glucopyranoside (**69**).

To a solution of **68** (0.48 g, 1.13 mmol), phthalimide (0.93 g, 6.30 mmol), and triphenylphosphine (1.57 g, 6.0 mmol) in dry THF (40 mL) diethyl azodicarboxylate (DEAD) (0.93 mL, 5.9 mmol) dissolved in dry THF (5 mL) was added dropwise and the reaction was stirred at room temperature under N_2 for 72 h. The solvent was evaporated *in vacuo* and the residue dissolved in CH_2Cl_2 (50 mL) was washed with brine and dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification of the residue with ethyl acetate - hexane (8:2) eluent afforded the product (1.0 g, 94%, R_f 0.28 EtOAc - hexane; 7:3). $[\alpha]^{24}_D$ +28.5 (c 1.0, $CHCl_3$); MS (FAB): 966 $(M+Na)^+$, 943 $(M)^+$; ^1H NMR(500 MHz, $CDCl_3$): δ 1.91-1.98 (m, 8H, 4 $OCH_2CH_2CH_2NPht$), 3.06-3.11 (m, 2H, H-4, H-2), 3.29 (s, 3H, OCH_3), 3.43 (t, 1H, $J_{3,4}$ 9.5 Hz, H-3), 3.46-3.63 (m, 8H, 4 $OCH_2CH_2CH_2NPht$), 3.65-3.92 (m, 11H, 4 $OCH_2CH_2CH_2NPht$, H-5, H-6, H-6'), 4.70 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1), 7.45-7.80 (16H, m, 4 ArH); ^{13}C NMR (62.9 Hz, $CDCl_3$): 28.8, 29.3, 29.4, 29.6 ($OCH_2CH_2CH_2NPht$), 35.3, 35.7, 35.8

($OCH_2CH_2CH_2NPht$), 54.9 (OCH_3), 68.7, 69.2, 69.8, 70.0, 70.6, 71.0, 76.5 ($OCH_2CH_2CH_2NPht$, C-5, C-6), 78.24 (C-4), 80.8 (C-2), 81.9 (C-3), 97.7 (C-1), 123.0, 123.1, 131.9, 132.0, 132.2, 132.4, 133.7, 133.8 (ArC), 168.2 (CONPht). Anal. Calcd for $C_{51}H_{50}O_{14}N_4$: C, 64.96; H, 5.34. Found: C, 64.68; H, 5.42.

1-O-Acetyl-2,3,4,6-tetra-O-3-phthalimidopropyl-α-D-glucopyranose (**70**).

A solution of **69** (1.0 g, 1.06 mmol) in acetic anhydride (10 mL) was stirred at -20 °C for 10 min. To this stirred solution was added precooled (0 °C) Ac_2O/H_2SO_4 (50:1, 5 mL) in 5 min, and the reaction mixture was left at -20°C for 3 days. The reaction mixture was diluted with dichloromethane (100 mL) and was washed successively with sat. $NaHCO_3$ (50 mL) and water (50 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo* and co-distilled with toluene several times. The residue was purified on silca gel column with ethyl acetate - hexane (7:3) solvent to yield a colorless oil (0.8 g, 78%; R_f 0.19); MS(FAB): 1104 $(M+Cs)^+$, 994 $(M+Na)^+$; ^1H NMR(500 MHz, $CDCl_3$): δ 1.91-1.95 (m, 8H, 4 $OCH_2CH_2CH_2NPht$), 2.10 (s, 3H, OAc), 3.14-3.19 (2H, m, H-4, H-2), 3.40 (m,1H, H-3), 3.45 (m, 1H, H-6), 3.51-3.79 (m, 17H, H-6', 4 $OCH_2CH_2CH_2NPht$, 3.82-3.90 (m, 2H, H-3, H-5), 6.12 (1H, d, $J_{1,2}$ 3.5 Hz, H-1), 7.45-7.80 (m, 16H, 4ArH); ^{13}C NMR (62.9 Hz, $CDCl_3$): δ 21.0 (Ac-C-1) 28.8, 29.2, 29.4, 29.5 ($OCH_2CH_2CH_2NPht$), 35.3, 35.6 ($OCH_2CH_2CH_2NPht$), 68.5, 69.3, 69.3, 70.9, 71.1, 72.8, 76.5 ($OCH_2CH_2CH_2NPht$, C-5, C-6), 77.5 (C-4), 79.7 (C-2), 81.6 (C-3), 89.6 (C-1), 123.0, 123.1, 131.9, 132.0, 132.2, 132.3, 133.7, 133.7 (ArC), 168.2 (CONPht). Anal. Calcd for $C_{52}H_{50}O_{15}N_4$: C, 64.32; H, 5.19. Found: C, 64.41; H, 5.22.

2,3,4,6-Tetra-O-3-phthalimidopropyl-α/β-D-glucopyranosyl azide (**71**).

A solution of **70** (0.44 g, 0.45 mmol) in dry CH_2Cl_2 (20 mL) was stirred with azidotrimethylsilane (0.15 mL,

1.13 mmol) and tin(IV)chloride (0.026 mL, 0.23 mmol) for 1 day. The solution was diluted with dichloromethane (20 mL) and washed with 1M KF solution (10 mL) then with water (10 mL). The organic extract was dried ($MgSO_4$), filtered, and concentrated to afford a white foam (0.36 g, 83%; R_f 0.30 EtOAc-hexane; 7:3). $[\alpha]^{24}_D$ +51.8 (c 1.0, $CHCl_3$); MS(FAB): 977 $(M+Na)^+$, 955 $(M+1)^+$; ^1H NMR(500 MHz, $CDCl_3$): 1.89-1.97 (m, 8H, 4 $OCH_2CH_2CH_2NPht$), 3.06-3.15 (m, 2H, H-2, H-4), 3.29 (t, 1H, $J_{2,3}$ 9.0 Hz, H-3), 3.44-3.87 (m, 19H, H-5, H-6, H-6', 4 $OCH_2CH_2CH_2NPht$), 5.36 (1H, d, $J_{1,2}$ 3.5 Hz, H-1), 7.45-7.80 (m, 16H, 4 ArH). Anal. Calcd for $C_{50}H_{47}O_{13}N_7$: C, 63.47; H, 4.97. Found: C, 63.41; H, 4.88.

2,3,4,6-Tetra-O-3-phthalimidopropyl-α/β-D-glucopyranosylamine (**72**).

The azido sugar **71** (0.38 g, 0.4 mmol) dissolved in ethyl acetate (10 mL) was hydrogenated using Pd (10% on charcoal, 90 mg, 10%) catalyst for 2 days at room temperature. The catalyst was filtered off and washed with ethyl acetate (40 mL) and the filtrate was evaporated. The residue was purified with ethyl acetate-ether (9:1) eluent containing 0.5% triethylamine. The product (280 mg, 76%; R_f 0.21) is a white foam; MS (FAB): 951 $(M+Na)^+$, 928 $(M)^+$; ^1H NMR(500 MHz, $CDCl_3$): δ 1.84-1.99 (m, 8H, 4 $OCH_2CH_2CH_2NPht$), 3.01-3.11 (m, 3H, H-4, H-2, H-3), 3.44-3.92 (m, 19H, H-5, H-6, H-6', 4 $OCH_2CH_2CH_2NPht$), 4.95 (t, 1H, H-1), 7.45-7.80 (m, 16H, 4 ArH); ^{13}C NMR(62.9 Hz, $CDCl_3$): δ 28.7, 28.9, 29.4, 29.6 ($OCH_2CH_2CH_2NPht$), 35.4, 35.7 ($OCH_2CH_2CH_2NPht$), 69.3, 70.0, 70.2, 70.4, 70.8, 71.0, 75.6 ($OCH_2CH_2CH_2NPht$, C-5, C-6), 78.6 (C-4), 84.1 (C-2), 85.9 (C-3), 89.3 (C-1), 123.1, 131.88, 132.4, 133.5, 133.6, 133.7 (ArC), 166.2 (CONPht). Anal. Calcd for $C_{50}H_{49}O_{13}N_5$: C, 64.72; H, 5.32. Found: C, 64.41; H, 5.12.

*2,3,4,6-tetra-O-3-phthalimidopropyl- N-{1-(R/S)-[acetyl*amino]dodecyl}*-α/β-D-glucopyranosylamide* (**73**).

The amino sugar **72** (140 mg, 0.15 mmol) was coupled with tbutoxycarbonylaminododecanoic acid according to the procedures in example 3 above to yield the Boc protected lipoaminoacid-sugar conjugate. This material was treated according to the methods described in example 6 to provide the corresponding free amino compound. Acetylation with acetic anhydride (17 mg, 1.7 mmol) in dry CH_2Cl_2 (5 mL) overnight in the presence of triethylamine (2 eq) followed by removal of the solvents *in vacuo* and column chromatography with $CHCl_3$-MeOH (93:7) yielded the desired product (130 mg, 84%).

2,3,4,6-tetra-O-3-aminopropyl- N-{1-(R/S)-[*acetyl*amino]dodecyl}-*α/β-D-glucopyranosylamide* (**74**).

Compound **73** above is treated with ethylenediamine in dichloroethane at reflux for 18 hours. After this time, the solvents are reoved in vacuo and the product dissolved in acetonitrile/water/acetic acid. The crude product mixture is separated by ion exchange chromatography and the fractions lyophillised to dryness. The resultant compound is a lipoaminoacid - sugar conjugate bearing 4 amino functions.

It will be apparent to the person skilled in the art that while the invention has been described in some detail for the purposes of clarity and understanding, various modifications and alterations to the embodiments and methods described herein may be made without departing from the scope of the inventive concept disclosed in this specification.